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ORIGIN AND EVOLUTION OF THE CEREBELLUM*

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The cerebellum is knit in with the neuromotor apparatus of the body in diverse ways in different groups of vertebrates, and a survey of some of its generalized and aberrant forms may point the way to a better understanding of the mammalian type. If we can discover what functional factors were primitively concerned in the initial differentiation of the cerebellum from preexisting bulbar structures and some of the steps by which additional functional systems of diverse kinds were drawn into the cerebellar complex, some light may be shed on the great problems of the analysis of higher cerebellar functions. The accumulated data of comparative anatomy, embryology and physiology furnish the materials for such a survey and for tentative conclusions.

This summary is perforce presented largely in terms of comparative anatomy. The legitimate demand for experimental control of physiologic inferences drawn from known structural arrangements can receive meager satisfaction, for only fragmentary data are available. But under proper control the anatomic method can contribute much toward the functional analysis of the central nervous system. Starting from those primary sensory and motor centers the functions of whose direct peripheral connections have been experimentally determined, the patient unraveling of the related central conduction pathways has put in our hands a considerable amount of knowledge of structural relations whose functional meanings can be deduced, indirectly to be sure, yet with a high degree of probability. For instance, knowing something of the functions of the vestibular nucleus, we can safely infer that any remote part of the nervous system that receives fibers originating within this nucleus participates in the vestibular functions. This method has already filled many of the gaps in our fragmentary knowledge of cerebral function derived from direct experiment.

As applied to the cerebellum, this method has yielded considerable accurate information regarding the kinds of sensory excitation which are discharged into the cerebellum by its afferent tracts, and something

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about the regional distribution within the cerebellum of these functional systems. We have also some less detailed and accurate information regarding the sources within the cerebellum of its efferent tracts and their distribution to various lower motor centers.

These anatomic observations have considerable physiologic value as indicative of the raw materials from which the intrinsic cerebellar functions are fabricated, but of themselves they give us no direct evidence of the actual functional patterns of these intrinsic activities. Only actual experiment or carefully controlled clinico-pathologic observations can answer these questions. But even in this field the known structure of the cerebellar cortex sheds valuable light on the results of functional examination, as witnessed by the apparatus of "avalanche conduction" as described by Ramón y Cajal in relation to the tonus effects of the cerebellum, to which reference is made later.

Comparative anatomy, however, does not always follow physiology; it sometimes points the way. In the hands of Bolk, it has already served a useful purpose in stimulating experimental work and directing the search for evidence of localization of cerebellar functions by new methods.[1]

THE AMPHIBIAN CEREBELLUM

Our description will begin with *Amphibia* because in some of these species, and probably in tadpole stages of all of them, there is seen a functioning cerebellum of more generalized and apparently of more primitive type than is found elsewhere. The structure of the cerebellum in the simplest adult amphibians is similar to that of the lowest true vertebrates, the cyclostomes, and is even more generalized.

So exceedingly rudimentary is the cerebellum of some of the tailed amphibians that by several comparative anatomists this organ is said to be totally absent.[2] This is not the case, but the minute cerebellum of these generalized amphibians is instructive. In the American mudpuppy, Necturus, this has been examined;[3] and in the larval stages of salamanders and frogs the history of the differentiation of the amphibian cerebellum is tolerably closely recapitulated. The amphibian tadpoles are hatched in an immature condition, so that in following their subsequent development it is possible to watch the growth of the cerebellum as a functioning organ almost from its first appearance.

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1. Van Rynberk, G.: Das Lokalisationsproblem im Kleinhirn, Ergeb. der Physiol. **7**:653-698, 1908.

2. Edinger, L.: Vorlesungen über den Bau der nervösen Zentralorgane, Leipzig, Ed. 6. **2**:127, 1908. Bindewald, C.: Eine Commissura intertrigemina im Amphibiengehirn, Anat. Anz. **40**:243-247, 1911.

3. Herrick, C. Judson: The Cerebellum of Necturus and Other Urodele Amphibia, J. Comp. Neurol. **24**:1-29, 1914.

Cutaneous sense organs of the lateral line system and their nerves are present in early larval stages of both lower and higher Amphibia and in adults of permanently aquatic forms. The nerves from these widely distributed organs all converge to enter the dorsolateral border of the medulla oblongata in company with those from the internal ear. In the tailed forms (urodeles) the common terminal nucleus of all of these fibers, or octavolateral area, borders the rhomboidal lip throughout nearly the whole extent of the fourth ventricle.[4] This area curves around the wide lateral recess of the fourth ventricle to invade its upper or rostral border, which is the cerebellum (Fig. 1). In the simpler types, there is no cerebellar tissue developed in the mid-dorsal plane between these two cerebellar thickenings, with the exception of some commissural and decussating fibers.

The isthmus is a region of retarded development in the neural tube, for here no important cranial nerve roots have their nuclei. Accordingly, the rhomboidal lip in this region is not under the dominant physiologic influence of any single functional system of peripheral nerves. This transitional and physiologically indifferent tissue is favorably located for receiving and elaborating nervous impulses from all primary sensory centers which are significant in the execution of proprioceptive reactions.

Here the rostral end of the octavolateral area is directly continuous across the isthmus with the roof of the midbrain, where are located the visual centers, the mesencephalic nucleus of the fifth nerve and important correlation centers for the lateral line, auditory, somesthetic and tactual systems, all of which are significant collaborators with the vestibular system in the maintenance of equilibratory and postural reflexes. Into this transitional region, that is the medial part of the upper lip of the lateral recess, spinocerebellar tracts are discharged, thus contributing the remaining components essential for the fabrication of a true cerebellum.

Adult Necturus possesses a cerebellum which, although reduced to the lowest terms compatible with its recognition as such, exhibits the essential cerebellar structure and connections. It consists of a pair of slight thickenings of the upper (rostral) walls of the lateral recesses of the fourth ventricle which receive at their lateral borders direct root fibers of the eighth and lateral line nerves, secondary fibers from the octavolateral areas, and (more medially) fibers from the spinal cord, midbrain roof and probably hypothalamus. Its gray matter contains Purkinje cells of simple form, but no true granules have been observed. The efferent fibers are axons of the Purkinje cells, which distribute

4. Herrick, C. Judson: The Medulla Oblongata of Larval Amblystoma, J. Comp. Neurol. **24**:343-427, 1914. Also Footnote 3.

to the motor tegmentum in the same way as do those from the octavolateral area farther spinalward—tractus cerebellotegmentalis. Under the cerebellar thickening of each side there is a slight ventricular eminence in the rostral wall of the lateral recess, the ventral eminence of the cerebellum, whose large cells form the nucleus cerebelli and give rise to fibers of the tractus cerebellotegmentalis. Other fibers from this eminence and from the more ventral parts of the body of the cerebellum proper are directed ventralward and forward as brachium conjunctivum. The nucleus cerebelli is clearly the precursor of the roof nuclei and dentate nuclei.

Young tadpoles of the salamander, *Amblystoma tigrinum*, show a cerebellum of similar form and internal structure, as illustrated in Figure 1, drawn from a wax model of the cerebellar region of a specimen 20 mm. long.

In following the development of the cerebellar region in larvae of *Amblystoma tigrinum*, it is found that in specimens 8 and 10 mm. in length the major divisions of the brain are well defined, but the cerebellum has not made its appearance. Below the isthmus there is a sharp dilation of the ventricle, thus marking the site of the future lateral recess, but the widest part of the fourth ventricle is farther back at the level of the roots of the fifth nerve. At the level of the eighth root there is a small octavolateral thickening just below the rhomboidal lip.

At 12 mm. the lateral recess has greatly widened, the octavolateral area is in process of differentiation forward into the lower or caudal wall of the recess, and the cerebellum has definitely made its appearance in its upper or rostral wall. This cerebellum is probably functional, for the related fiber tracts are well developed; and from this stage onward to the adult there is merely progressive elaboration of the pattern here present.

The lateral expansion of the early neural tube between the isthmus and the fifth roots, that is, the formation of the lateral recess, appears to be correlated with the development in this region of extensive mechanisms of sensorimotor correlation. In *Amblystoma* all sensory root fibers of the fifth, seventh and eighth systems bifurcate on entering the medulla, and one of the resulting branches ascends into this territory, where connections are made with the underlying motor tegmentum. From the researches of Coghill, it is known that functional connections of this type are effected in this region long before the beginning of cerebellar differentiation.

At a later period (beginning at about 10 mm. stages in our specimens) the border of the rhomboidal lip in the region of the lateral recess is progressively thickened from two directions. From behind, a massive thickening of the octavolateral area pushes forward from its

In all illustrations, *a. ac.* indicates octavolateral area; *a. ac. a.*, octavolateral area, anterior lobe; *a ac. p.*, octavolateral area, posterior lobe; *aq.*, aqueduct of Sylvius; *a. V.*, area trigemini; *br. conj.*, brachium conjunctivum; *cb. m. d.*, dorsal median body of cerebellum; *c. cb.*, corpus cerebelli; *com. cb.*, cerebellar commissure; *con. l. l.*, concrescence of lateral lobes; *cor. pin.*, corpus pineale; *cr. cb.*, cerebellar crest; *d. v.*, decussatio veli; *em. cb. v.*, ventral cerebellar eminence (nucleus cerebelli); *em. gr.*, eminentia granularis; *em. V.*, area trigemini; *hyth.*, hypothalamus; *l. m.*, lateral lemniscus; *lob. au.*, auricular lobe; *mes. V.*, mesencephalic root of the fifth nerve; *nuc. cb.*, nucleus cerebelli; *nuc. mes. V.*, nucleus of mesencephalic fifth nerve; *Nuc. VIII.*, nucleus of the eighth nerve; *nuc. VII, l. l. d.*, dorsal lateral line nucleus of the seventh nerve; *nuc. VII, l. l. v.*, ventral lateral line nucleus of the seventh nerve; *nuc. VII m.*, motor nucleus of the seventh nerve; *pl.*, choroid plexus; *r. III.*, root of third nerve; *r. IV.*, root of fourth nerve; *r. IX.*, roots of ninth nerve; *r. l.*, recessus *lateralis; r. l. l.*, roots of lateral line nerves; *r. sp.*, roots of first spinal nerve;

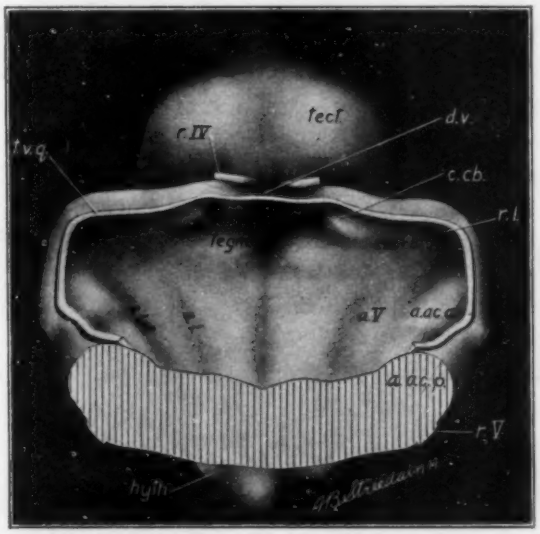
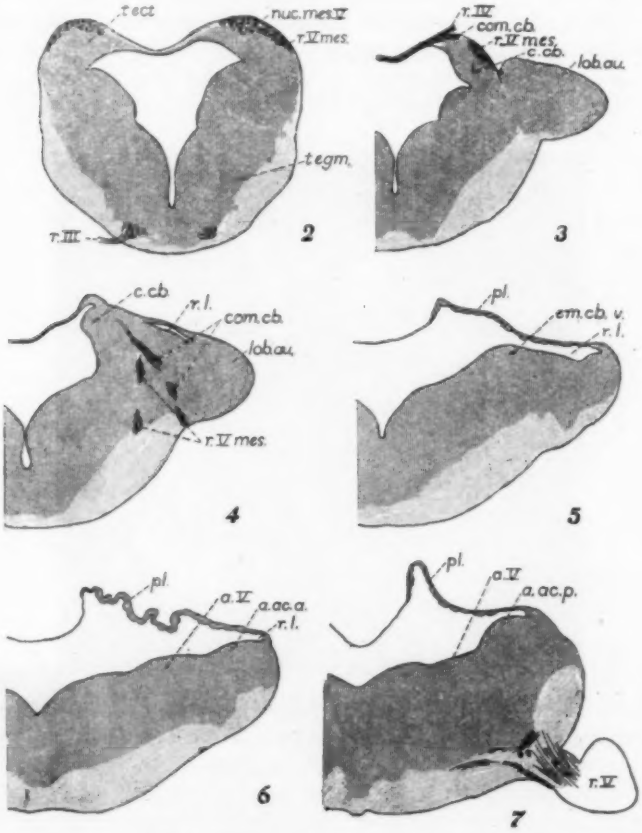


Fig. 1.—A wax model of the cerebellar region of a 20 mm. larva of Amblystoma tigrinum. The specimen is seen from behind and slightly from above so as to look under the overarching body of the cerebellum into the lateral recesses. By reason of the angle from which the model is viewed the forth ventricle appears greatly foreshortened in the cephalocaudal direction. × 62.

r. V., roots of fifth nerve; *r. V mes.*, mesencephalic root of fifth nerve; *r. VI.*, roots of sixth nerve; *r, VII.*, roots of seventh nerve; *r, VII l. l. d.*, dorsal lateral line root of seventh nerve; *r. VII l. l. v.*, ventral lateral line root of seventh nerve; *r. VII mot.*, motor root of seventh nerve; *r. VIII.*, root of eighth nerve; *r. X*, roots of vagus nerve; *s. l.*, sulcus limitans; *s. lat.*, sulcus lateralis; *st. a.*, stratum album; *st. g.* stratum griseum; *tect.*, tectum mesencephali; *tegm.*, tegmentum; *tr. mes. cb. ant.*, anterior mesencephalocerebellar tract; *tr. mes. cb. p.*, posterior mesencephalocerebellar tract; *tr. sp. cb*, spinocerebellar tract; *tr. sp. t.*, spinotectal tract (spinal lemniscus); *t. v. q.*, taenia of fourth ventricle; *val. cb.*, valvula cerebelli; *v. cb.*, cerebellar ventricle; *v. 4*, fourth ventricle.

initial site at the level of the eighth root to invade the lower wall of the lateral recess (Fig. 1, *a. ac. a.*), and from in front the cerebellar thickening (Fig. 1, *c. cb.* and *em. cb. v.*) similarly builds up in the upper or rostral wall of the recess. At the 20 mm. stage, as illustrated in Figure 1, these two thickenings have not yet joined, though they are in close approximation. During this period of rapid differentiation the lateral recess is greatly widened, apparently as a mechanical result of the peculiar mode of growth of the rhomboidal lip; that is, the pro-



Figs. 2 to 7.—A series of cross sections through the region of the cerebellum from larval Amblystoma 20 mm. long. × 62.

Fig. 2.—Section through the midbrain.

Fig. 3.—Section through the decussatio veli at the junction of the body of the cerebellum with the midbrain.

Fig. 4.—Section through the auricular lobe at its widest part.

Fig. 5.—Section through the lateral recess and ventral eminence of cerebellum.

Fig. 6.—Section through the rostral ends of the octavolateral area and area trigemini.

Fig. 7.—Section through the superficial origin of the fifth nerve.

gressive thickening of the upper and lower walls of the recess leaves the wall thinner and weaker at the extreme lateral angle between the two thickenings and the lip crumples at that point, thus forming the auricular lobe of the medulla oblongata. These relations are illustrated in cross section by Figures 2 to 7.

At 20 mm. the cerebellum has become massive laterally, but it does not reach the middorsal plane except for fibers of the cerebellar commissure, with which are associated fibers of the fourth nerves and mesencephalic fifth roots. The body of the cerebellum forms the upper wall of the lateral recess (Figs. 3 and 4 *c.cb.*) and the ventral cerebellar eminence, containing the nucleus cerebelli, forms the adjacent floor (Fig. 5, *em. cb. v.*). Laterally there is a great differentiation of cerebellar tissue, and of the auricular lobe (Figs. 3 and 4), with which in later stages the rostral end of the octavolateral area is intimately fused and into which sensory root fibers of the trigeminal, vestibular and lateral line nerves penetrate.

The cerebellum of adult *Amblystoma* [5] is considerably more massive and more compact than in Necturus. Dorsally the two lateral thickenings which form the body of the cerebellum of the larva are confluent above the ventricle, and ventrally the nucleus cerebelli (primordial deep nuclei) is more deeply embedded within the cerebellar substance than in the larva. Histologically, well defined Purkinje cells and granules are present, although of simpler form than in mammals. The granular layer is absent in the mid-dorsal region, and it increases progressively in thickness toward the lateral border. The lateral recess of the larva has been largely filled by an accumulation of granule cells (the so-called eminentia granularis) so that the auricular lobe would appear on casual inspection to be solid. This, however, is not the case, for the lateral recess of the fourth ventricle extends outward and forward to cover the whole dorsolateral aspect of the auricular lobe (Figs. 8, *A, B* and *C, r.l.*), the roof of this diverticulum of the lateral recess being a choroid plexus (*pl.*). The thick granular layer of the auricular lobe is, therefore, not superficial, but here, as elsewhere, it borders a ventricular surface. Root fibers of the vestibular, lateral line and trigeminal nerves extend far forward, almost to the rostral end of the auricular lobe. These relations are important for the interpretation of the more highly differentiated types of cerebellum, for the auricular lobe is the parent tissue of the floccular parts in higher animals.

The cerebellum of the frog has been recently restudied by Larsell.[6]

5. Larsell, O.: The Cerebellum of Amblystoma, J. Comp. Neurol. **31**:259-282, 1920.

6. Larsell, O.: The Cerebellum of the Frog, J. Comp. Neurol. **36**:89-112, 1923.

The development follows closely that of the salamander already described. During metamorphosis of the tadpole the lateral line organs and nerves disappear, with resultant shrinkage in the relative size of the auricular lobe, although this part retains its connection with root fibers of the vestibular nerve. The lateral recess is more completely filled by the eminentia granularis than in *Amblystoma,* although even here the granule cells of this eminence are not truly superficial, for as in Amblystoma (Fig. 8) a fold of the choroid plexus of the fourth ventricle extends forward to a point beyond the rostral end of the eminence, whose entire lateral border is thus a ventricular surface.[7] In other respects the differences between the cerebellum of an adult frog and *Amblystoma* are matters of degree only, the former possessing a more massive cerebellar body and more highly differentiated tissue elements. The spinocerebellar tract and its cerebellar connections have assumed increased importance in correlation with the more powerful and more mobile limbs of the frog.[8]

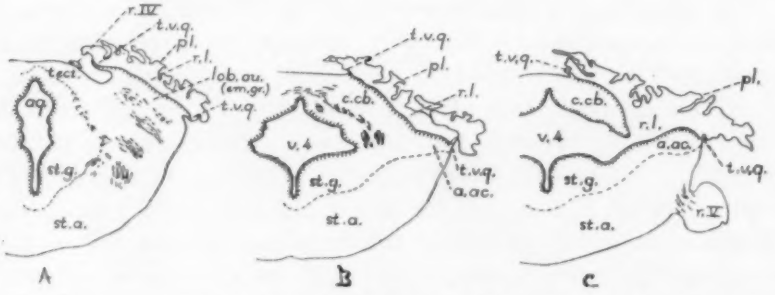


Fig. 8.—Transverse sections through the cerebellum of adult Amblystoma. × 14. For details of internal structure see Figures 21, 19 and 17 of Larsell's paper (J. Comp. Neurol. **31**:276-277, 1920) which were drawn from the same preparations. *A,* section through the auricular lobe (*lob. au.*) near its rostral end to illustrate the forward extension of the lateral recess (*r. l.*) and choroid plexus (*pl.*) which cover its external surface; *B,* section through the most massive part of the cerebellum; *C,* section through the posterior end of the cerebellum.

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7. A brief reference to this anterior diverticulum of the lateral recess is made in a description of the brain of the bullfrog by Kappers and Hammer: Das Zentralnervensystem des Ochsenfrosches (Rana catesbyana), Psych. en Neurol. Bladen, 1918, Feestbundel Winkler, pp. 368-415. Here it is stated that its walls are in front enclosed on all sides by nervous material, as in urodeles. This is certainly not the case in our specimens of old larvae, toward the close of metamorphosis, of *Rana catesbiana* or of adult *Rana pipiens.* In these cases the lateral wall of the recess is plexiform throughout, and a fold of this choroid plexus extends forward at the side of the midbrain far beyond any part of the massive cerebellum or auricular lobes.

8. Kappers, C. U. A.: Vergleichend Anatomie des Nervensystems der Wirbeltiere und des Menschen, Haarlem, 1921.

From this review of the structure and development of the amphibian cerebellum, it appears that the definitive organ has a twofold origin. Two centers of differentiation appear in the rhomboidal lip on opposite sides of the wide lateral recess, and the functional factors involved in the elaboration of these two regions can be clearly read. The lip in the lower border of the lateral recess thickens from behind forward, and this is nothing other than a differentiation of the rostral end of the octavolateral area, for root fibers of the vestibular and lateral line nerves run throughout its entire extent. From this thickening is developed the greater part of the massive auricular lobe with its contained eminentia granularis. With the loss of the lateral line fibers in adult frogs and higher vertebrates, this region comes to be dominated by vestibular fibers, and from it the floccular region of the mammalian cerebellum is derived.

The thickening of the rhomboidal lip in the upper border of the lateral recess takes place under the influence of a different group of functional connections—optic, acoustic and somesthetic fibers from the adjacent roof of the midbrain and spinocerebellar fibers of proprioceptive type. Since the latter fibers early become the dominant members of this complex, it is of interest to observe the steps in their elaboration.

At the time when the cerebellum first makes its appearance in *Amblystoma* (between the 10 mm. and the 12 mm. stages in our specimens), there is already present a connection between the spinal cord and the roof of the midbrain, the spinotectal tract. At a later period some of these fibers push forward into the thalamus, thus forming a true spinal lemniscus. As these fibers cross the isthmus to enter the midbrain, they pass under the cerebellum, and here some of them turn medialward and dorsalward into the cerebellum as the spinocerebellar tract. Some of these spread throughout the body of the cerebellum of the same side, and a large compact fascicle crosses in the cerebellar commissure to distribute similarly on the opposite side. But as late as midlarval stages this spinocerebellar tract is not completely separate from the spinotectal and spinothalamic tracts.

I have observed [9] that, as the common ascending tract passes under the cerebellum, spinocerebellar fibers separate from it in two ways. The more ventral fibers are independent spinocerebellar elements, but from the more dorsal fibers of the spinotectal system collateral branches are given off which also enter the body of the cerebellum. Similar collaterals are given off farther spinalward to enter the correlation centers of the medulla oblongata. These relations are shown diagrammatically in Figure 9.

9. Herrick, C. Judson: J. Comp. Neurol. **24**:374-376, 1914.

This can only mean that at this stage of development the exteroceptive and proprioceptive nervous impulses ascending from the spinal cord are imperfectly differentiated from each other. From the common ascending tract some nervous impulses are filtered off for various bulbar reflexes; others are filtered off into the cerebellum, where they come into physiologic relationship with vestibular and other proprioceptive systems; others continue forward into the midbrain and thalamus, where they effect various reflex connections of exteroceptive type. As a result of this integration of ascending spinal impulses with those from the ear and other sense organs of especial proprioceptive significance, a new type of central adjustment comes into play—the cerebellar functions are born.

We thus see that the definitive amphibian cerebellum originates within the rhomboidal lip partly in front of and partly behind the lateral recess of the fourth ventricle; that these two regions early come under the dominant influence of different functional connections (the first, or body

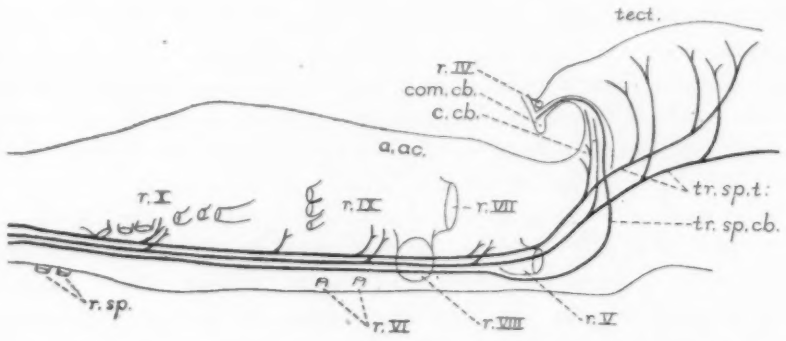

Fig. 9.—Lateral profile of the medulla oblongata of a 38 mm. larva of Amblystoma tigrinum, with diagrammatic representation of the courses of the spinocerebellar and spinotectal tracts (Herrick: J. Comp. Neurol. **24**:343-427, 1914).

of the cerebellum, by the spinocerebellar system, the second, or auricular lobe, by the vestibulolateral system); and that in later development they fuse into a single massive organ. These two regions, moreover, in higher vertebrates retain something of their distinctive physiologic characteristics, becoming in one case the median cerebellar mass and in the other case the lateral floccular part.

These two component parts of the cerebellum are in intimate physiologic connection by various systems of intrinsic neurons, and the right and left halves of the organ are broadly connected by a complex system of commissural and decussating fibers which form the cerebellar commissure. Even in the simplest known forms these conditions prevail, as illustrated by *Necturus* (Fig. 10).

The efferent fibers of the cerebellum primitively pass from all parts of its substance into the underlying motor tegmentum (cerebellotegmental fibers); but even in the simplest amphibian form there is a region below the medial cerebellar body from which arise fibers which can be recognized as brachium conjunctivum (Fig. 10). This region is the ventral eminence, containing the nucleus cerebelli.

In the simpler *Amphibia* the cerebellar cortex is in a rudimentary condition. Here, as elsewhere in these brains, all the cells retain their embryonic position as central gray. In *Necturus* rudimentary Purkinje cells can be recognized, but no granules. In this small organ, each Purkinje cell seems to receive directly all of the kinds of nervous impulses which enter the cerebellum, converging these into its axon,

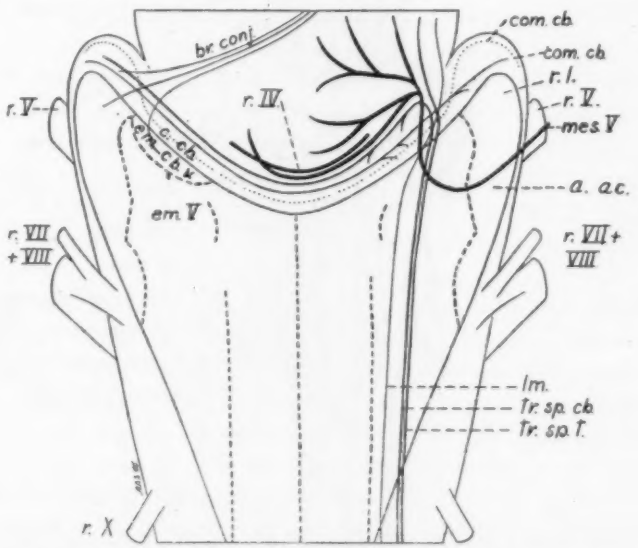

Fig. 10.—Diagram of some of the cerebellar tracts of Necturus and the composition of the decussatio veli containing the cerebellar commissure.

which discharges either directly into the motor tegmentum or into the ventral nucleus cerebelli.

With increase in the size of the cerebellum as we pass to higher Amphibia, the Purkinje cells approach the typical mammalian form, and definitive granules arise from undifferentiated elements. In the frog, the granules are numerous, especially at the lateral borders, and they evidently play an important part in the diffusion of nervous impulses throughout the larger organ.

FISHES

Cyclostomes.—The lowest of the true vertebrates, the cyclostomes, possess a cerebellum whose organization is in the main similar to that of

the lower *Amphibia,* although perhaps more primitive.[10] The chief afferent tracts come from the octavolateral area, which is incompletely differentiated from the underlying trigeminal area. It receives other fibers from the roof of the midbrain and from the hypothalamus. A spinocerebellar tract is regarded by Clark [11] as probably present, although not actually demonstrated. The neurons of this cerebellum resemble those of the octavolateral area; they are modified in the direction of Purkinje cells and granule cells without, however, attaining this grade of differentiation.

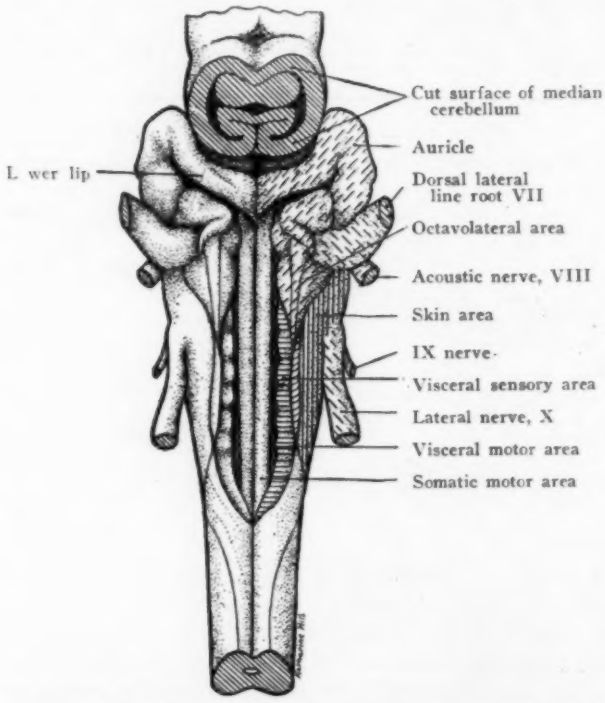

Fig. 11.—The medulla oblongata of Squalus acanthias seen from above after removal of the membranous roof of the fourth ventricle. The posterior part of the dorsal median body of the cerebellum has been cut away to expose the lower lip. × 2. (Modified from Herrick's "Introduction to Neurology.")

In the lateral border of the cerebellum of the lamprey (Petromyzon) where it joins the octavolateral area, there is a group of large cells called by van Höevell nucleus octavomotorius anterior, which he regards

10. Johnston, J. B.: The Brain of Petromyzon, J. Comp. Neurol. **12**:1-86, 1902. Tretjakoff, D.: Das Nervensystem von Ammocoetes. II. Gehirn. Arch. mikr. Anat. **74**:636-779, 1909.

11. Clark, W. B.: The Cerebellum of Petromyzon fluviatilis, J. Anat. Physiol. Series 3, **1**:318-325, 1906.

as the representative of the front portion of the lateral vestibular nucleus of Deiters. Their axons form a cerebellotegmental bundle, some going forward to decussate under the nuclei of the third nerves. These seem to represent the brachium conjunctivum. From his description, it seems probable that this is the nucleus cerebelli; it may also be true that it includes a part of Deiters' nucleus.

The indications are that from an ancestral type not far from that of *Petromyzon* the forms of cerebellum of various groups of vertebrates have diverged, and that in all sluggish forms, especially those which typically rest on their bellies and therefore require little elaboration of equilibratory adjustments and motor control in general, this differentiation is retarded.

Elasmobranchs.—In the sharks (Fig. 11) the octavolateral area is highly developed, curving around the dilated lateral recess of the fourth ventricle to form the so-called auricle of this brain (sometimes improperly termed corpus restiforme). The anteromedial ends of the areas of the two sides fuse in the midplane over the fourth ventricle, thus forming a part of the cerebellum known as the lower lip, which in form resembles the medial part of the organ in cyclostomes and amphibians, although it is not functionally equivalent. This is seen in Figure 11 immediately below the cut surface of the large median body of the cerebellum.

The lower lip and the auricles are paired structures and will here be termed the lateral parts of the cerebellum in distinction from the much more massive dorsal unpaired medial part which overlies them and is commonly called the body of the cerebellum. Vestibular and lateral line root fibers enter the lower or ventral lobes of the auricles, and the remainder of the auricles and the lower lip seem also to be concerned chiefly with vestibulolateral adjustments.

In comparison with the more generalized cyclostomes and amphibians, the dorsal median body of the elasmobranch cerebellum seems to be a new structure; and so it is, but its origin can readily be traced, for the median body receives the large spinocerebellar tracts and also fibers from the inferior olives, midbrain and hypothalamus, that is, it is developed in response to the enlargement and segregation of the nonvestibular functional systems. In *Amphibia,* the auricular lobes are dominated by the vestibulolateral system, but the more medial body of the cerebellum receives fibers of these and all other afferent systems in a single undifferentiated field. In elasmobranchs, the vestibulolateral field is of the same form as in amphibians, namely, the auricular lobes and lower lip, but from the latter part the remaining afferent fiber tracts are detached to enter the newly differentiated dorsal median body.

The auricle of the brain of the shark is much larger than the amphibian auricular lobe, but its form is essentially the same, being an

enlargement of the rhomboidal lip on both upper and lower sides of an extensive lateral recess which is roofed throughout by choroid plexus. All parts of the auricles and lower lip that are visible in Figure 11 are ventricular surfaces. The median body of the cerebellum is an enlargement and dorsal evagination of the dorsal wall between the tenia of the fourth ventricle and the decussation of the fourth nerves, as is clearly seen in Figure 12.

In the cortex of the dorsal median body, there are highly differentiated granule and Purkinje cells. In the auricles, as in *Amphibia*, there are also immense accumulations of granules. Efferent fibers which are closely similar to those from the related octavolateral area leave the auricles for the underlying motor tegmentum. From the dorsal body of the cerebellum axons of some Purkinje cells pass directly to the

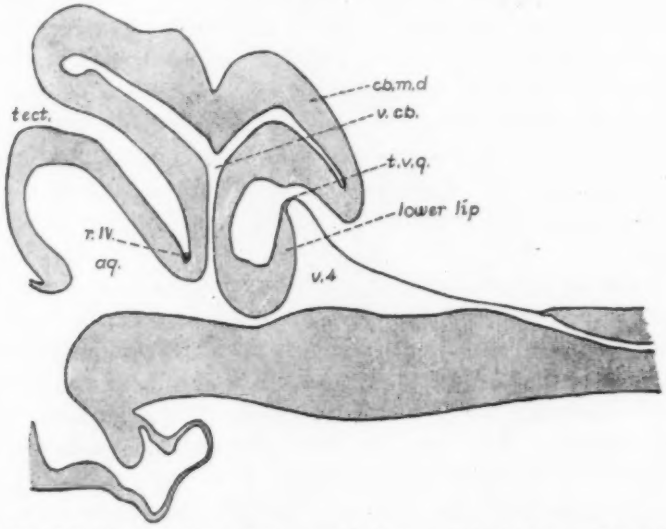

Fig. 12.—Median section of the cerebellum of Acanthias. Modified from van der Horst: Das Kleinhirn der Crossopterygii, Bijdragen tot de Dierkunde, Amsterdam, 1919.

motor tegmentum of the medulla oblongata and midbrain; others go to a laterally placed nucleus cerebelli, from which fibers of the brachium conjunctivum arise, much as in *Amphibia*. That the dorsal body of the cerebellum of the dogfish is physiologically independent of the vestibular apparatus, has been experimentally confirmed by Tilney.[12]

To recapitulate, the elasmobranch cerebellum presents two parts which are structurally and functionally well defined: (1) the paired auricles and lower lip, that is, the vestibulolateral field, comparable with

12. Tilney, F.: Genesis of Cerebellar Functions, Arch. Neurol. Psychiat. 9:137-169 (Feb.) 1923.

the mammalian flocculus and related structures; and (2) the dorsal median body, comparable very roughly with the mammalian vermis and concerned chiefly with proprioceptive reactions of the somesthetic and optic systems.

Ganoids and Teleosts.—The cerebellum of the simpler cartilaginous ganoids, like the sturgeon, is small, resembling externally that of the salamander, but internally there are notable differences. Of these the most noteworthy feature is the addition of a new median cerebellar lobe, in this case not evaginated dorsally, as in sharks, but invaginated and thrust forward into the ventricle of the midbrain, as illustrated in Figure 13. This is the valvula. There is also an extensive spread of cerebellar tissue of transitional type spinalward beyond the lateral recesses, the cerebellar crests, which cover the dorsal surfaces of the octavolateral areas. These rostral and caudal extensions of cerebellar tissue are greatly enlarged in the bony fishes. in connection with which they will be further considered.

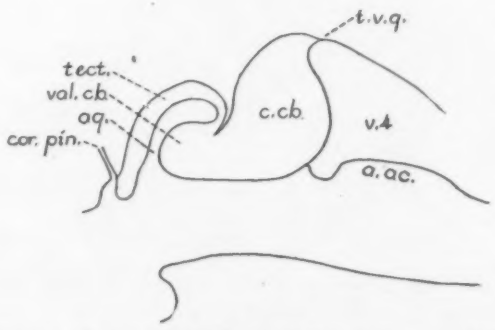

Fig. 13.—Diagram of the cerebellum of the sturgeon, *Acipenser*, in parasagittal section.

From ancient generalized fishes of the pre-Devonian period with a cerebellum probably comparable with that of the present day sturgeon, the steps in the transition to the extraordinarily complicated and diverse organs of the bony fishes can readily be followed in living intermediate species, and these steps are recapitulated in the embryonic development of the higher forms.

From Schaper's excellent description [13] of the development of the trout, we learn that in an embryo fifty-seven days after fertilization of the egg the more rapid growth of the rhomboidal lip in the region of the lateral recess has resulted in the formation of a cerebellum of the form seen in the adults of *Petromyzon* and the lower *Amphibia*. In

13. Schaper, A.: Die morphologische und histologische Entwicklung des Kleinhirns, Morph. Jahrb. **21**:625-708, 1894.

subsequent stages, the walls of the lateral recess, comparable with the auricle of the shark, are at first accelerated in development, and the medial part is retarded. Later these relations are reversed, and the medial parts grow more rapidly. There are two of these median enlargements, both of which in some species of teleosts attain enormous dimensions. There is, first, a dorsal evagination which produces a median cerebellar body comparable with that of elasmobranchs, and second, a ventral growth directed forward into the ventricle of the midbrain, the valvula. Figure 14 illustrates a median section through the cerebellum of a trout six months old.

The adult teleostean cerebellum is more compact than the selachian and very differently organized internally. In forms like the cod, in which it is moderately developed, we note the following features: The dorsal median body has fibrous connections and functions which are essentially similar to those of elasmobranchs. The walls of the embryonic

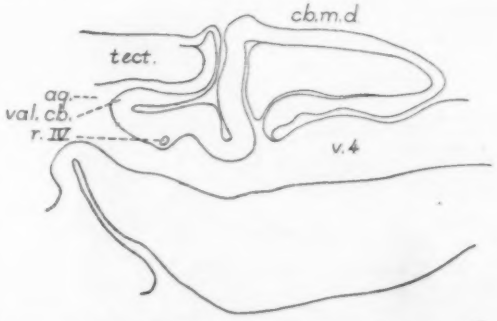

Fig. 14.—Median section of the cerebellum of the trout six months after fertilization of the egg. Modified from Schaper.

lateral recess have coalesced, and this space is completely filled with granule cells, forming the so-called eminentia granularis. In some forms, as in the catfishes (*Amiurus, Silurus*), the eminentia granularis forms a prominent lateral lobe which in position and functional connections is like the auricle of sharks. It is, however, a solid mass of superficial granules not enclosed by an extension of the fourth ventricle with a covering of choroid plexus, as in the frog. This granular mass extends forward under the optic lobes into continuity with the valvula. The two granular eminences are connected across the caudoventral border of the body of the cerebellum by a mass of granules (the pars postrema) which resembles the lower lip of sharks, the whole structure being the primary vestibulolateral part of the cerebellum.

From this vestibulolateral part three more or less extensive prolongations of cerebellar tissue of related physiologic type are directed, a median one forward as valvula cerebelli and a pair of lateral ones backward as cerebellar crests. In some species the crests of the two

sides are greatly enlarged and fuse above the fourth ventricle, forming the concrescence of the lateral lobes (Fig. 15). The cerebellar crest is in the closest possible relations with the terminal area of the vestibular and lateral line nerves, and its functions are evidently subsidiary to those of this area.

The valvula is a median structure which grows forward into the midbrain ventricle from a point in the isthmus where the two lateral cerebellar plates (which in the early embryo form the upper borders of the lateral recesses) join above the ventricle. It may be greatly enlarged, as in *Megalops* (Fig. 15); and in *Mormyrus* and allied fishes from the Nile it attains amazing dimensions, dilating the mesencephalic ventricle and mushrooming out so as to envelop nearly all of the rest of the brain. In this fish the ratio of the size of the valvula to that of the rest of the brain is probably larger than the ratio of the size of the human cerebral

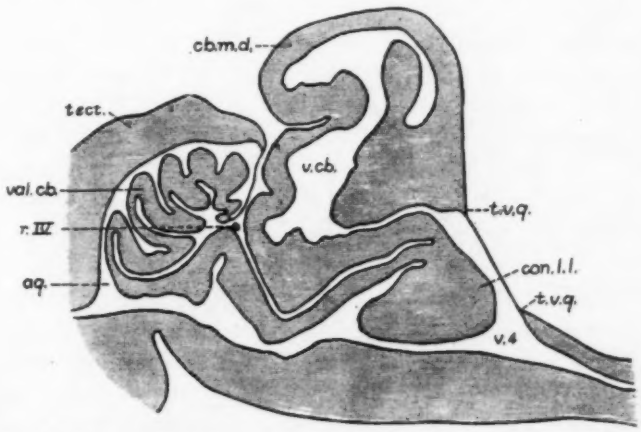

Fig. 15.—Median section of the cerebellum of a teleost, Megalops cyprinoides. Modified from van der Horst.

hemispheres to the brain stem. This enlargement seems to be colligated directly with an increase in the size and complexity of the lateral line centers of the medulla oblongata and midbrain, although we do not yet know the exact functional significance of this connection.

Fibers from the midbrain enter the teleostean cerebellum in two groups: (1) an anterior system from the optic centers in the midbrain roof ending chiefly in the body of the cerebellum—obviously an optic-cerebellar system; and (2) a posterior system from mesencephalic correlation centers of the lateral line nerves (nucleus lateralis valvulae of the torus semicircularis) terminating chiefly in the valvula (Fig. 17). Each of these systems distributes more widely than this, but these are clearly their characteristic connections.

The teleostean valvula can now be interpreted physiologically. Recent studies [14] have made it plain that its size varies in correlation with the elaboration of the sense organs of the lateral lines, their related peripheral nerves and cerebral centers. Enlargement of these nerves in teleosts goes hand in hand with increase in their bulbar centers and the overlying cerebellar crest and also with the differentiation of a special correlation center of this system in the deeper parts of the midbrain roof, contiguous to which the valvula is developed, and of the valvula itself.

Notwithstanding great differences in external form, the functional subdivision of the teleostean cerebellum conforms in general plan with that of elasmobranchs. The vestibulolateral part includes the cerebellar crests, the eminentia granularis of each side, the connecting "pars

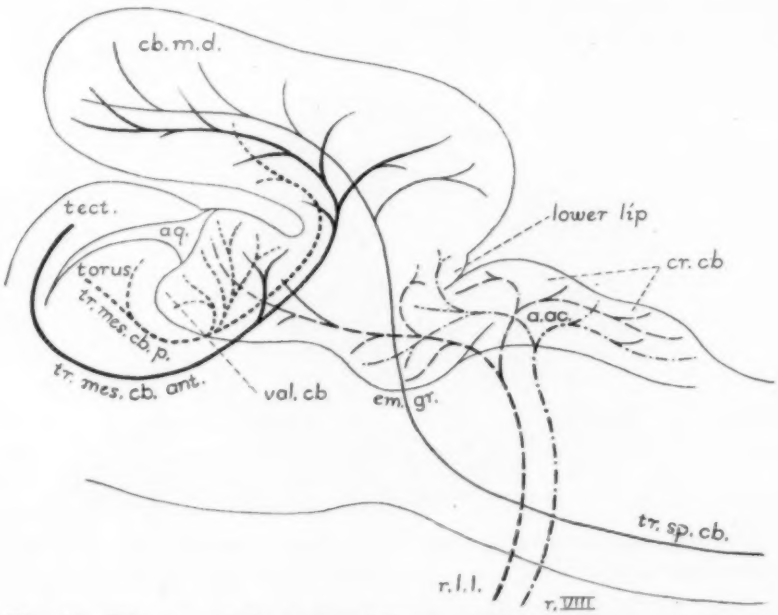

Fig. 16.—Diagram of the parts of the cerebellum and some of the related fiber tracts of the catfish, Amiurus, seen as projected on the median plane. Fiber tracts related to the octavolateral sensory system are drawn in broken lines. The connection between the octavolateral area of the medulla oblongata (*a. ac.*) and the midbrain (*torus*), that is, the lateral lemniscus, is not drawn.

postrema" and the valvula. The dorsomedian body, as in elasmobranchs, is the optic and somesthetic part, receiving the large spinocerebellar and olivocerebellar tracts, also fibers from the optic centers of the midbrain and others (of unknown function) from the hypothalamus. This func-

14. Van der Sprenkel, Berkelbach: The Central Relations of the Cranial Nerves in Silurus glanis and Mormyrus caschive, J. Comp. Neurol. **25**:7-63, 1915.

tional localization in terms of the distribution of afferent systems of fibers is only approximate, and it varies greatly from type to type, but it is believed that the foregoing statements express the general relationships. The efferent paths are essentially as in elasmobranchs.

This functional analysis of the teleostean cerebellum has recently been subjected to further control by Addison,[15] who makes a comparison of the relative sizes of the fiber tracts connected with the cerebellum in three species of fishes. In the cod, with very large eyes and optic lobes, the anterior mesencephalo-cerebellar tract is very large; in catfishes and flatfishes with smaller eyes this tract is relatively smaller. In all cases it distributes mainly to the dorsal cerebellar body. The spino-cerebellar tracts (also terminating in the dorsal body) are larger in the two fishes last named, whose body and fin musculature are more elaborate than in the cod. The posterior mesencephalo-cerebellar tracts (distributed chiefly to the valvula) are large in catfishes, whose lateral line organs and nerves are large and complex.[16]

Summary.—The diverse and often bizarre forms assumed by the cerebellum in various fishes are instructive; for, taken in connection with the related fiber tracts, these local enlargements give the clues to a type of functional localization which is preserved in principle, although in much less spectacular form, in mammals.

Starting from the generalized form of cyclostomes, the sharks exhibit a great enlargement of two fundamentally different regions, a vestibulolateral part in the auricles and lower lip and a spinocerebral (somesthetic, optic) part in the median body. In ganoids and bony fishes the differentiation of the cerebellum has gone much further. The original vestibulolateral part has been incorporated into the massive cerebellum as a histologically distinct lateral and caudoventral region, and from this locus it has spread both backward and forward—backward as the cerebellar crest and forward as the valvula. The valvula has grown up in correlation with the differentiation within the midbrain of special correlation centers (poorly developed in sharks) related with the lateral line nerves. The dorsal median body of the teleostean cerebellum is concerned chiefly with spinal, optic and hypothalamic functional systems.

In land animals the lateral line system of sense organs and nerves disappears entirely, with a corresponding shrinkage of the vestibulolateral centers within the brain stem and cerebellum. The vestibular component of this complex, however, persists in relations which are fundamentally unchanged in all higher brains.

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15. Addison, W. H. F.: A Comparison of the Cerebellar Tracts in Three Teleosts, J. Comp. Neurol. **36**:1-35, 1923.

16. Van der Sprenkel, op. cit. Herrick, C. Judson: The Cranial Nerves and Cutaneous Sense Organs of the North American Siluroid Fishes, J. Comp. Neurol. **11**:177-249, 1901.

REPTILES AND BIRDS

The higher fishes which have last been considered are terminal members of the vertebrate phylum; they are not ancestral to any other forms. The reptiles were derived from primitive amphibian forms which are now extinct. In the reptiles of today the body of the cerebellum is enlarged as compared with any amphibians, although internally the plan is similar to that of the frog, with small vestibular parts laterally and a much larger spinal part in the median body. The principal efferent nucleus, which lies below the main cerebellar mass in urodeles (ventral cerebellar eminence) and in fishes lies far laterally, is here incorporated definitely within the cerebellar body.

In birds there is notable advance in size and complexity of organization, but again no fundamental departure from the sauropsid pattern as seen in reptiles. The functionally defined regions appear more clearly in mid-developmental stages than in the adult form. Ingvar's figure [17] of the cerebellum of a chicken of nine and one-half days' incubation shows a lateral recess and auricle in substantially the urodele form, the auricle becoming the flocculus of the adult, that is, the vestibular part. Vestibulocerebellar fibers end in this part and in the interfloccular region comparable with the lower lip of fishes at the posterior border of the cerebellum, a condition closely similar to that already described in fishes and reptiles.

The adult bird's cerebellum resembles in form the mammalian vermis and flocculi, there being no cerebellar hemispheres. Spinocerebellar tracts are well developed; their exact mode of ending in the cerebellum is variously described by different observers. According to Ingvar, they are distributed to the caudal and rostral parts of the body of the cerebellum, not to the flocculus or middle part of the body. The latter is regarded as phylogenetically younger than the more marginal parts and of different physiologic type.

The efferent systems show several special features. Axons of the Purkinje cells for the most part do not leave the cerebellum but terminate in the deep nuclei—roof nuclei and dentate nuclei. From the latter, the brachium conjunctivum arises; from the former, large cerebellospinal and cerebellobulbar tracts, including an important efferent connection with Deiters' nucleus in the vestibular area.

MAMMALS

With the advent of mammals, certain radical changes in cerebellar architecture are initiated. The avian flocculus is greatly enlarged, and to it is added a paraflocculus. The median body of the avian cerebellum

17. Ingvar, S.: Zur Phylo- und Ontogenese des Kleinhirns, Folia Neurobiol. **11**:205-495, 1918.

resembles the mammalian vermis, but is by no means exactly the same thing. And as we pass from lower to higher mammals, there is interpolated between the vermis and the floccular formation progressively more tissue of the cerebellar hemispheres, until in man the hemispheres overshadow everything else.

It does not lie within the scope of this paper to review the history of the further elaboration of the cerebellum within *Mammalia*. The literature of this field is extensive, and general agreement on all points has not been reached. But comment on a few general features will readily bring into view the broad lines of relationship between the more primitive types already discussed and the human organ.

The familiar history of the development of the human cerebellum runs parallel with that of the lower vertebrate orders,[18] and some of the earlier of these stages resemble in external form adult cerebella of lower types. Thus the form of the cerebellum of the human embryo of about 8 weeks is similar to that of adult *Amblystoma*, with the exception of the absence of the lateral line component in the rhomboidal lip below the lateral recess and corresponding reduction in size of this region.

The neuroblasts of the developing rhomboidal lip in the region of the lateral recess exhibit a series of remarkable pulses of activity. In the lower border of the lateral recess, the receptive nuclei of the eighth nerve develop in situ, and from this same part of the rhomboidal lip great numbers of proliferated neuroblasts migrate ventrally, some spinalward to form the inferior olive, others farther forward to form the nuclei of the pons and related gray centers, all of these structures being cerebellar dependencies. From the upper border of the lateral recess, parallel with the growth of the cerebellum, there is a similar extensive migration of neuroblasts, which in this case is directed dorsally to form the cerebellar gray matter.

In mammals the cerebellum as commonly described comprises five ill defined regions, a median vermis, paired lateral hemispheres, and ventrally the paired flocculi and paraflocculi; but these subdivisions do not correspond exactly with the significant physiologic and morphologic regions. Following the analysis of Ingvar,[17] we may say that viewed phylogenetically the mammalian cerebellum consists of an inferomarginal part which is ancient and probably comparable with the whole organ of lower orders, and a dorsal central part of more recent origin

18. My brother's account in 1891, of the embryonic development of the cerebellum, was the first clear demonstration of its bilateral origin and of the phylogenetic significance of the proliferations in the walls of the lateral recess. Herrick, C. L.: The Evolution of the Cerebellum, Science, Series 1, **18**:188-189, 1891; Contributions to the Comparative Morphology of the Central Nervous System. I. Illustrations of the Architectonic of the Cerebellum, J. Comp. Neurol. **1**:5-14, 1891.

which has been elaborated parallel with and in physiologic relationship with the cerebral cortex. The new or central part in the dorsal convexity of the organ is very small in the lowest mammals and is probably foreshadowed in birds, and in higher forms it increases in proportion to the enlargement of the cerebral cortex, until in man it comprises by far the larger part of the organ, as shown in Figure 17.

The inferior part of the old cerebellum (lingula, uvula, nodulus, flocculi) receives direct vestibular root fibers, as in lower forms; that is, the inferomarginal region is the vestibular part. Fibers from the spinal cord reach the remaining subdivisions of the old cerebellum, and also to some extent the marginal parts of the new cerebellum.

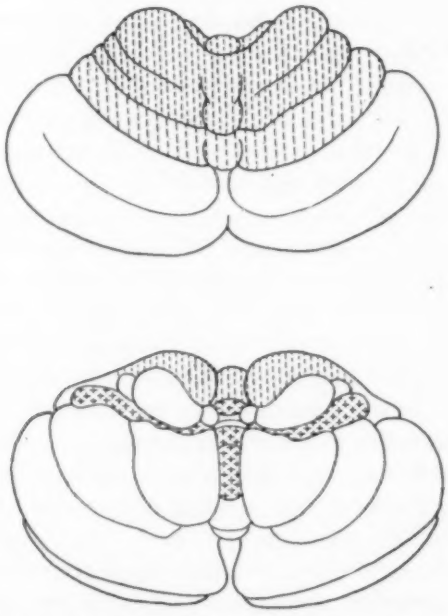

Fig. 17.—Sketches of the upper and lower aspects of the human cerebellum. On the basis of experimental operations on various animals, Ingvar is of the opinion that in the areas marked with crosses the cerebellar cortex receives direct fibers of the vestibular roots (in the cat flocculi, uvula, nodulus, lingula), and in the area shaded with broken lines the cortex receives spinocerebellar fibers. These two shaded areas comprise the old cerebellum; the unshaded areas are of later phylogenetic origin (the new cerebellum) developed largely in correlation with corticopontile fibers from the cerebral hemispheres. In man the exact limits of the fields here designated are as yet unknown.

The new part is developed in correlation with the cerebral cortex with which it is in functional relation through the pons and otherwise, probably regulating movements of cortical origin in much the same way that other parts of the cerebellum regulate the simpler reflexes arising

from vestibular excitation, muscle sense and other proprioceptive receptors.

The sources of the efferent cerebellar fibers of the guinea-pig have recently been reexamined by Allen.[19] No axons of Purkinje cells leave the cerebellum except a few from the vermis to the lateral vestibular nucleus (of Deiters). All others terminate in the deep cerebellar nuclei, and the lateral vestibular nucleus seems to show some characteristics, both histologic and physiologic, which ally it with the deep cerebellar nuclei. The deep nuclei comprise two functionally different groups: (1) The medial nucleus fastigii, which receives direct vestibular root fibers, fibers from the vestibular nucleus, from the cortex of the vermis and (probably) from the basal vestibular cortex. Its efferent fibers are distributed to the nuclei of the medulla oblongata and midbrain (cerebellobulbar tracts). (2) The nuclei dentatus, emboliformis and globosus form a lateral group, which receives fibers from the cerebellar cortex (chiefly from the hemispheres) and gives rise to the brachium conjunctivum.

SOME GENERAL CONSIDERATIONS

Definition of cerebellum.—No review of the extensive literature on the comparative anatomy and physiology of the cerebellum will be here attempted. From the morphologic side this is well summarized in Kappers' comparative anatomy of the nervous system to which reference has already been made, and in the preceding pages some works especially relevant to this discussion are mentioned. Tilney's recent survey of the genesis of cerebellar functions, already cited, opens an interesting perspective, with, however, so incomplete an analysis of what is known of the cerebellum of lower vertebrates as to be in some respects misleading.

Tilney's "cerebellum bulbare" includes in lower vertebrates our octavolateral area and in mammals only the vestibular nucleus. The inclusion of the primary vestibular nucleus in the cerebellum is inconsistent with his own definition of the cerebellum as a suprasegmental structure; and he has overlooked the interesting transition of the rostral differentiated part of the octavolateral area into the auricle and flocculus. The flocculus of birds is incorrectly regarded as a new structure ("cerebellum laterale") which is considered, also incorrectly, to be the place of origin of the lateral cerebellar lobes or hemispheres of mammals. His cerebellum jugale includes the body of the cerebellum of *Petromyzon* and what we have called the lower lip of fishes, with the equivalent of the latter in higher forms. The cerebellum mediale comprises the vermis of birds and mammals (except the inferior part or cerebellum jugale) and in fishes what we have termed the dorsal median cerebellar body.

19. Allen, William F.: Distribution of the Fibers Originating from the Different Basal Cerebellar Nuclei, J. Comp. Neurol. **36**:399-439, 1924.

In its broadest features, Tilney's outline of the evolution of cerebellar functions has much to commend it, but as applied in detail it is so at variance with the well-known organization of the various species considered as to require critical revision.

A comparison of the present discussion with Tilney's essay raises the question, Exactly what do we mean by cerebellum? It has just been stated that the primary vestibular nucleus should be excluded, and this in the face of the well-known fact that root fibers of the vestibular nerve are widely distributed within the cerebellum in all classes of vertebrates.

The distinction between vestibular nucleus and the vestibular field of the cerebellum is admittedly hard to draw, and indeed in some lower forms this is impossible. But there are obvious functional as well as structural contrasts between these in their definitive forms. The vestibular nucleus is concerned with simple sensorimotor adjustments in which the afferent impulses come exclusively or chiefly from the internal ear (plus the related lateral line organs in fishes and amphibians). In regions where to these afferents there are added much larger numbers of nervous impulses of other functional systems through the intrinsic neurons of the cerebellar cortex, the structure can no longer be called a primary nucleus but a part of the cerebellum. One might say that as soon as any part of the field of distribution of vestibular root fibers acquires functional connections with other proprioceptive systems in sufficient number to act chiefly as an apparatus of coordination and integration of these diverse factors, it may be called cerebellum—as exemplified by the auricle of fishes and the flocculus of mammals.

This functional criterion has an easily recognized anatomic expression in the fabrication of cerebellar cortex, whose histologic features are in broad lines similar throughout the vertebrate phylum. In those fishes in which the cerebellar crest overflows on the octavolateral area and covers its entire dorsal surface, the texture of this structure is intermediate between that of typical vestibular nucleus and typical cerebellar cortex. This is a reflection of its ambiguous functional character, for the crest receives both vestibulolateral root fibers and fibers of other functional significance from the cerebellum, the former giving its dominant character. The mammalian flocculus also receives both kinds of fibers, but here the vestibular fibers are subordinate and the tissue is unequivocal cerebellum.

Functional Factors in Morphogenesis.—Reviewing the vertebrate series, the general plan of cerebellar differentiation is seen to be simple and to follow naturally in correlation with certain broad lines of functional relationships. The vestibular nucleus was primitively the chief center of physiologic dominance of the equilibratory reactions and probably also a chief center of dominance for tonus, exerting more or less regulatory control over the local tonus mechanisms (described by Sher-

rington and others) in lower neuromotor systems. There is abundant experimental evidence that the vestibular apparatus exerts a direct control over muscular tone, and the tonic functions of the cerebellum, on which so much stress is laid by recent physiologists, are apparently elaborations of this primitive characteristic of the parent tissue out of which the cerebellum has developed.

In the simplest living vertebrates the octavolateral area extends within the rhomboidal lip throughout almost the entire length of the medulla oblongata, and in all fishes and aquatic amphibians the fibers of the lateral line nerve roots enter this area dorsally of the eighth fibers, as shown in Figure 18. Just what may be the functional relationship between lateral line sense organs and semicircular canals is not yet clear; but from the structural arrangement of the centers of these two sensory systems in the medulla oblongata and cerebellum, it is obvious that their functions are intimately intertwined, and in most fishes the lateral line

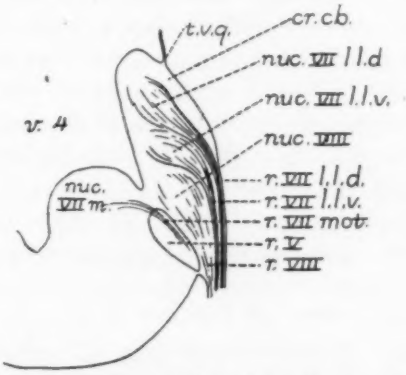

Fig. 18.—Diagrammatic cross section through the medulla oblongata of Petromyzon at the level of the seventh and eighth roots. The sensory nuclei of the fifth, seventh and lateral line nerves are arranged in vertical series, the phylogenetically older members lying ventrally and the younger dorsally (Johnston). The cerebellar crest (*cr. cb.*), here rudimentary, is greatly enlarged in teleosts, and farther rostrally the entire cerebellum occupies a corresponding position with reference to the underlying structures.

components of this complex play the larger part in shaping the configuration and internal structure of the cerebellum.

It is known experimentally that in fishes, as in men, the eyes cooperate with the semicircular canals in the maintenance of equilibrium and posture. The rostral end of the octavolateral area primitively lies adjacent to the caudal end of the visual area in the roof of the midbrain, and this middle ground, which is not dominated by either system, is the primordial cerebellum. This territory receives additional fibers from all other parts of the central nervous system which can participate in proprioceptive reactions, and these systems are very diverse in accord-

ance with the mode of life of the species. Chief among these added afferent systems are the spinocerebellar fibers, whose importance increases progressively with the elaboration of the musculature of the trunk and limbs.

In the simplest known types of cerebellum the lateral (auricular) parts are dominated by the vestibulolateral connections, and the more medial cerebellar body of each side receives both these and other proprioceptive systems. With increase in the importance of the spinocerebellar system the dorsal median cerebellar body is detached from the primitive bilateral cerebellar body, and in higher fishes there is a more or less elaborate marginal vestibulolateral cerebellum, on which is superposed the dorsal nonvestibular part, these being kept in functional relationship by a complex of intrinsic neurons. In land animals, the lateral line components drop out, leaving the "old cerebellum" of reptiles and birds very simply organized on the plan just outlined.

Parallel with the unfolding of the cerebral cortex in mammals there is another localized pulse of differentiation in the cerebellum, namely, the formation of the "new cerebellum," which is a functional dependency of the cerebral cortex. This in turn makes its first appearance in the dorsal convexity of the old cerebellum, and as it enlarges it forms the larger part of the superior vermis and the hemispheres, finally crowding the old cerebellum downward into an obscure position.

The morphogenetic factors which have operated in building up the cerebellum obviously comprise three functionally and structurally defined groups: afferent systems, efferent systems and intrinsic systems of nervous conduction.

1. The afferent systems. These may be considered under three heads as already defined: first, the primordial vestibular and vestibulolateral systems, distributed in mammals to the marginal parts, i.e., those nearest to the parent tissue of the brain stem from which the cerebellum was elaborated; second, the mesencephalic and spinal systems, distributed more dorsally; third, the neopallial systems, again in higher vertebrates reaching the upper surface farther dorsal than the last.

These three afferent systems of fibers distribute within the cerebellar cortex in an arrangement that is roughly concentric, the two more recently differentiated fields in each case arising in the center of the preexisting territory and expanding dorsally, as has been emphasized by Ingvar. The cerebellar cortex, accordingly, shows an ill defined functional localization determined by the distribution within it of these physiologically diverse systems of afferent fibers—ill defined, because there is considerable overlap of the cortical fields reached by these fiber systems.

2. The efferent systems. Primitively each of the cerebellar neurons was both receptive and emissive. In fishes and amphibians generally

the axons of the primordial Purkinje cells (or some of them) provide the efferent path, these arcuate fibers taking courses similar to those from the primary octavolateral area. But special efferent neurons comparable with those of the roof nuclei and dentate nuclei of higher forms have been recognized in all of these animals in the nucleus cerebelli near the point of junction of the primitive body of the cerebellum with the octavolateral area. As the vertebrate series is ascended, these efferent neurons become more distinctly segregated and more deeply embedded in the cerebellar gray at its ventrolateral border, and finally this collection of cells is resolved into the medial roof nuclei (fastigii) and the more lateral group (globosus, emboliformis and dentate nuclei), the latter growing proportionally to the cerebellar hemispheres within which they lie.

The gradual transition from the primitive nucleus cerebelli to the roof nuclei and dentate nuclei has been sketched by Kappers in his great work on the comparative anatomy of the nervous system, and Baron van Höevell [20] in a more extended discussion expresses the belief that the nucleus cerebelli in its most primitive form is only a forward continuation of the lateral vestibular nucleus of Deiters.

It is generally recognized that the receptive apparatus of the cerebellum, that is its cortex, has arisen in close structural and functional relations with the primary vestibular sensory nucleus; it now appears that its efferent apparatus, that is the deep nuclei, shows a similar relationship. In this connection one is reminded of Malone's [21] recent argument that the so-called sensory nuclei of the brain stem combine both sensory and motor functions, and that this two-fold nature is reflected in the histologic structure of their neurons in many cases. In the vestibular nucleus, for instance, we find small cells of the sensory type with finely divided chromophilic substance, and in addition the larger elements of the motor type with coarse deeply staining chromophilic granules in the nucleus of Deiters. It is generally agreed that the latter are in much more direct functional connection with the motor apparatus than are the former.

If the deep nuclei of the cerebellum are genetically related with the lateral efferent elements of the vestibular nucleus and the cerebellar cortex with the more specifically receptive parts of the vestibular nucleus, the numerous points of similarity between cerebellar and vestibular functions are readily accounted for.

We may conclude that there is on the efferent side of the cerebellum of mammals an obscure functional localization which, like the afferent,

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20. Höevell, J. L. D. van: The Phylogenetic Development of the Cerebellar Nuclei, Proc. kon. Akad. Wetensch., Amsterdam **18**:1421-1434, 1916.

21. Malone, E. F.: The Cell Structure of the Superior Olive in Man, J Compt. Neurol. **35**:205-211, 1923.

may be defined in terms of the anatomic connections of the related fiber tracts. In mammals the efferent fibers directed toward the lower motor centers of diverse groups of synergic muscles appear to arise from different parts of the complex of deep cerebellar nuclei. The fact that the origin of these fibers is subcortical explains the difficulty in the demonstration of localized motor functions by electric stimulation of the cerebellar cortex.

These two localization patterns, defined respectively in terms of afferent and efferent systems of fibrous connections, are not coextensive. They appear to be to some extent independent variables whose patterns are determined in the first case by the sensory equipment of the species in question and in the second case by the organization of the motor mechanisms. The teleosts manifest the most diversified and extreme differentiation of the sensory systems colligated with equilibrium and posture, with a corresponding amplification of the cerebellar cortex in localized regions, each of which is related with a particular group of sensory systems (dorsal cerebellar body, valvula, lower lip, auricular lobes, cerebellar crest). Yet the muscular systems of these animals are in all cases relatively simple, and the efferent cerebellar apparatus is correspondingly simply organized. In birds and mammals, on the other hand, where the afferent tracts from the primary sensory centers are less extensive than in most teleosts but the motor mechanisms of the trunk and limbs are far more complex, the efferent nuclei of the cerebellum show a correspondingly more complex structural and functional differentiation.

3. The intrinsic elements. Notwithstanding detailed descriptions of the Purkinje cells, granules, basket cells and other intrinsic neurons of the cerebellum, our knowledge of the exact connections of these elements is far from complete even in mammals; in lower forms the available descriptions are still less satisfying. But, as already suggested, the recorded facts of structure shed much light on the actual apparatus of cerebellar control of tone and posture.

The indications are that at the beginning of the series of forms here reviewed (cyclostomes) the first step in the differentiation of Purkinje cells and granules from an unspecialized type has been taken. The granule cells are always strictly intrinsic to the cerebellum, and in higher vertebrates numerous other types of intrinsic neurons are added. The Purkinje cells, moreover, are progressively transformed from elements each of which combines afferent and efferent functions (receiving the terminals of the afferent cerebellar fibers and discharging their axons into the motor tegmentum) into intrinsic elements whose axons do not leave the cerebellum. Parallel with this structural differentiation of its cortex there is increase in the influence exerted by the cerebellum in maintenance of muscular tone, posture and motor control.

The definitive cerebellar cortex exhibits a mechanism preeminently qualified to exert this tonic effect—apparatus for the wide diffusion of the afferent nervous impulses and their summation and reinforcement (avalanche conduction of Cajal), for the rapid and powerful discharge of large batteries of Purkinje cells (which, as Malone has pointed out, structurally tend toward the motor type), and for the distribution of the efferents from the latter cells to specific synergic systems of lower motor centers through an elaborate switch-board type of organization of the deep cerebellar nuclei.

In the matter of intrinsic localization of cerebellar functions, the observations of Bolk in a hitherto unexplored field of comparative anatomy prepared the way for an extensive series of experimental and clinical studies which are still in process.

Cerebellar Localization.—The preceding remarks about localization of function within the cerebellum are based primarily on the structural arrangement of the related fiber tracts, whose connections within and without the cerebellum are more or less well known. The physiologic inferences naturally drawn from these arrangements, of course, require experimental confirmation or emendation. Adequately controlled experimental work on cerebellar functions of lower vertebrates is scanty, and the conclusions so far reached are rather vague and inharmonious.[22] The purpose of this sketch is to suggest that what is known about the "functional connections" of the cerebellum and the historical development of these connections may assist in the formulation of the physiologic problems and in devising more fruitful methods of experimental approach.

The classical methods of study of localization of function in the cerebral cortex when applied to the cerebellum have been rather barren of helpful results. The relations of these two kinds of cortex to the brain stem appear to be fundamentally different; it follows that different experimental technic is required. The anatomic evidence suggests that any functional localization that may be present in the cerebellar cortex is an expression of differences in the spatial distribution of afferent fibers from physiologically different lower centers; this is a matter for which an adequate experimental control can be devised.

The histologic pattern of the cerebellar cortex is substantially the same in all fields. There is no structural mosaic of cortical patterns like that of the cerebral cortex, and there is little experimental evidence

22. The earlier experimental work on the cerebellum of fishes is summarized with new observations by Polimanti, O.: Contributi alla fisiologia del sistema nervoso centrale e del movimento dei pesci, Zool. Jahrb. **30**:473-716, 1911. Some later experiments are published by Reisinger, L.: Die zentrale Lokalisation des Gleichgewichtssinnes der Fische, Biol. Centralbl. **35**:472-475, 1915.

of specific functional differences between the intrinsic activities of the several cerebellar cortical fields. These intrinsic functions seem to be of like nature throughout its extent. Structurally the cerebellar cortex is adapted for the spread and intensification of any nervous impulses which are discharged into it. These functions are expressed physiologically primarily in changes in tone, and all experimentally demonstrated cerebellar functions are thought by some physiologists to be various manifestations of this influence.[23]

These tonic and sthenic functions appear to be exhibited in substantially the same way throughout the extent of the cerebellar cortex. It is immaterial whether the afferent impulses come in directly from the semicircular canals, from terminal nuclei of fibers of muscle sense within the spinal cord, or from the cerebral cortex; once having reached the cerebellar cortex, their further intracortical progress seems to be similar in all of these cases. How this cerebellar activity will express itself in behavior is determined, not by the specificity of the afferent impulses alone nor of the regions of cerebellar cortex excited, but by the nature of the total sensorimotor activity at the moment in process in the subcerebellar apparatus.

The cerebellum contains no primary centers for the regulation of any bodily movements. These are amply provided elsewhere. If, as Sherrington says, it is "the head ganglion of the proprioceptive system," this implies that it modifies and integrates the activities of the lower proprioceptive mechanisms without usurping any of the simpler reflex functions intrinsic to the local apparatus.

Really fruitful study of localization of function within the cerebellum is still in its infancy. As naturally follows from the preceding considerations, the most promising approaches to the problem are indirect, such as the influence of the cerebellum on motor activities in process, on decerebrate rigidity and on tonus in general.[24] Normally the cerebellum is constantly in receipt of countless afferent impulses from the periphery and from all parts of the central nervous system which are active in maintaining tone, posture and motor control in general.

23. This implies a step-up of energy potential within the cerebellum. Its cortex may be thought of as containing large latent reserves of chemically unstable material set on a trigger. Appropriate excitation releases this latent energy, which is then transmitted to such lower motor apparatus as may at the moment be in process. In a recent work entitled "Neurological Foundations of Animal Behavior" (Henry Holt & Co., New York, *in press*) I have discussed the mechanisms of correlation and coordination from this point of view (see especially Chapter XIX).

24. A promising experimental approach to such problems as are here under consideration has been suggested by A. Bickel: Untersuchungen über den Mechanismus der nervosen Bewegungsregulation, Eine Experimentell-klinische Studie, Stuttgart, 1903.

These afferents exhibit a coarse localization pattern in the cortex, as already indicated. There is a limited amount of experimental evidence that the excitation, narcosis or ablation of these cortical fields will affect those subcerebellar neuromotor processes with which they are in functional relationship, and these effects may be expected to differ according to the cortical field affected and according to the degree of the injury or depression or excitation. The same considerations apply to the deep nuclei and their efferent pathways. These too are matters readily subjected to further experimental control.

In all cases the essential nature of the activities intrinsic to the cerebellar cortex itself may be substantially the same in all of its parts. This is in marked contrast with the cerebral cortex, in which there is both anatomic and physiologic evidence of great diversity in the functions intrinsic to the various cortical areas.

Conclusion.—The cerebellum does not appear to participate in the analysis of sensory impressions for determining what the appropriate response shall be; but after the character of the response has been established, unconsciously in lower centers or consciously in the cerebral cortex, the cerebellum participates in the execution of the movements. Its own activities are wholly unconscious. According to this view of the matter the cerebellar functions broadly considered are coordinations rather than correlations in the sense in which I have elsewhere defined these terms.[25]

The cerebellum functions not merely as a chain reflex in response to proprioceptive reports of bodily movements after they have happened, but the primary sensorimotor centers and the correlation centers (and especially the cerebral cortex) discharge collateral impulses into it, so that this adjustor can act in anticipation of the actual response and throw its own machinery into gear with all the lower motor apparatus necessary to execute it properly.

One may picture the situation in one case as if a given contraction of a muscle and tension on its tendon were reported back to the cerebellum through the spinocerebellar tracts with resulting activity of the cerebellar cortex adapted to reinforce the contraction of the muscle and inhibit that of its antagonist so as to maintain the appropriate movement or posture, or to facilitate the motor process in some other way, thus stabilizing, prolonging or readjusting the local intrinsic activity, posture or tone of the lower neuromotor unit. In the second case, one may say figuratively that activities of, say, the prefrontal cerebral cortex are discharged into the precentral gyrus, thus activating some particular system of motor neurons with resulting execution of a voluntary move-

25. Herrick, C. Judson: Introduction to Neurology, Ed. 3, Philadelphia, W. B. Saunders Company, 1922, p. 36.

ment; and while this cerebral activity is in process the frontal cortex also activates the corticopontile path, sending this message into the cerebellum: "I am about to leap forward, get set, and cooperate in the movement." By the time the appropriate lower motor centers are activated through the pyramidal tract the cerebellar influence has become effective on these lower centers, with resultant improvement in the strength and efficiency of the movement.

In conclusion, I will quote a paragraph from the "Neurological Foundations of Animal Behavior," to which reference has already been made.

> The relationships in higher vertebrates of the centers of the brain stem, the cerebellum, and the cerebral cortex may be illustrated somewhat crudely by the analogy of the departments of the national government. The correlation centers of the brain stem correspond with the legislative branch of government, determining in advance by virtue of their innate organization what actions may appropriately be performed in each particular type of frequently recurring situation. The subcortical centers of coordination comprise the administrative department, attending to the execution of the acts which have been previously determined and initiated in the other departments of government. The cerebellum is a higher administrative bureau, supervising and coordinating the functions of certain of the executive offices, with the aid of an extensive information service to which reports of the activities of these offices are sent both in advance of their execution and afterwards. The cerebral cortex is a sort of glorified judicial branch of government, integrating the total behavior by combining its elements into cooperative systems in view of all the factors of present and past experience, and with extensive powers of veto over inappropriate reactions which may have been inaugurated in the lower centers.

THE SPINAL FLUID SUGAR*

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In this paper are presented sugar estimations in 421 cases of mental and nervous disease, together with some observations on apparently normal persons.

Since 1852, when Deschamps and Bussy attempted to determine the nature of the reducing substance in the spinal fluid, medicine has been concerned with the significance and value of sugar estimations. Added impetus to the determination of the sugar in the spinal fluid as a clinical sign of importance was given by von Economo in 1917, when he published the first reliable statistics on the sugar content of the spinal fluid and on the chemistry of the blood in epidemic (lethargic) encephalitis. Since then, much work has been done on the nature, quantity, and significance of the reducing substance in the spinal fluid in various diseases, but little on the relation between the blood sugar and spinal fluid sugar. Mestrezat [1] Hopkins,[2] Fine and Myers,[3] Rieger and Solomon,[4] and Ino [5] have made comparative studies of the blood and spinal fluid sugars. These have been unsatisfactory because no attempt was made to regulate the diet, or to correlate the time at which the blood and spinal fluid specimens were taken.

TECHNIC

Technic.—The newer methods for the estimation of "sugar" in blood and spinal fluid make it necessary to review critically our previous standards of normality. The quantitative determinations of sugar in the past have been made, as a rule, by one of three methods: that of Benedict, of Fehling or of

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1. Mestrezat, M.: Le liquide cephalo-rachidien, Paris, Maloine, 1912. L'examen clinique du liquide cephalo-rachidien, Gaz. d. hôp. **85**:789, 1912; J. de physiol. et pathol. **14**:504, 1912.

2. Hopkins, A. H.: The Sugar Content of Spinal Fluid in Meningitis and Other Diseases, Am. J. Med. Sc. **150**:847, 1915.

3. Fine, M. S., and Myers, V. C.: The Comparative Distribution of Urea, Creatinin, Creatin, Uric Acid, and Sugar in the Blood and Spinal Fluid, Proc. Soc. Exper. Biol. & Med. **13**:136, 1914.

4. Rieger, J. B., and Solomon, H. C.: The Sugar in Spinal Fluid, Boston M. & S. J. **175**:817, 1916.

5. Ino, I.: Experimental Studies on the Sugar in the Spinal Fluid, Act. Schol. Med. Univ. Imp. in Kioto **3**:609, 1919.

Bang. Schloss and Schroeder,[6] working exclusively on infants and children, and using Benedict's method, found that the normal spinal fluid sugar varied from 54 to 139 mg. per 100 c.c. Kopetski,[7] using the same method, found that the spinal fluid sugar varied from 48 to 53 mg. The Benedict method of sugar determination, however, gives a positive test when 50 mg. or more of sugar are present to every 100 c.c. of spinal fluid, the results being uniformly high.

Connall[8] based his observations on the sugar in health and disease, on qualitative determinations with Fehling's reagent, which yields unreliable results with the quantities of sugar present in the spinal fluid. Turner[9] used Fehling's quantitative method in his determinations, and the same is true of Kaplan.[10] Hopkins,[2] in an excellent paper, reports sugar findings in the spinal fluid determined by a method described by Bang, and Nawratzki[11] reports determinations made by Alliher's method. Not only have various methods been used in the determination of the spinal fluid sugar, but most of the methods have long been discarded. The determinations in this paper were made by a modification of the Benedict-Osterberg method for the determination of sugar in normal urine. Every determination was compared with that of another worker, however, who used the method of Folin. The results by these two methods varied only from 2 to 5 mg.

The Benedict-Osterberg technic modified by us for spinal fluid requires the following reagents: 0.6 per cent. picric acid solution, 5 per cent. aqueous sodium hydroxid, 50 per cent. aqueous acetone solution and a standard glucose solution (3 c.c. = 1 mg. glucose) from 1 to 2 c.c. of spinal fluid (as little as 0.5 c.c. may be used if necessary) is pipetted into a Folin-Wu sugar tube. To this is added 1 c.c. of a 0.6 per cent. picric acid solution and 0.5 c.c. of a 5 per cent. sodium hydroxid solution. The sides of the tube are then washed down with exactly 2 c.c. of water. Five drops of a freshly prepared 50 per cent. acetone solution are added, taking care that none of the solution touches the wall of the tube. A standard glucose is simultaneously prepared in the same way. Both tubes are placed in a boiling-water bath for from fifteen to twenty minutes. The tubes are then removed, cooled in a beaker of water, and diluted to 12.5 or 25.0 c.c. The standard is set at 15, the readings made in a colorimeter, and the calculations made as follows:

$$\frac{\text{Reading of Standard}}{\text{Reading of Unknown}} \times 10 = \text{per cent. of sugar in fluid.}$$

The solutions should be read within fifteen minutes after the completion of the test. We have omitted the use of bone black because determinations made on fluids with and without bone black gave the same results. Moreover,

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6. Schloss, O. M., and Schroeder, L. C.: The Nature and Quantitative Determination of the Reducing Substance in Normal and Pathological Spinal Fluids, Am. J. Dis. Child. **11**:1 (Jan.) 1916.

7. Kopetski, S.: Ztschr. f. Orenheilk. **68**:320, 1913.

8. Connall, Andrew: A Study of the Cerebrospinal Fluid in the Infective Diseases of the Meninges, Quart. J. Med. **3**:152, 1909.

9. Turner, B.: The Sugar in the Spinal Fluid, British M. J. **2**:60, 1918.

10. Kaplan, D. M.: The Laboratory Difference Between General Paresis and Cerebrospinal Syphilis, and the Serology of Cord Tumors, Am. J. Insan. **69**:337, 1912.

11. Nawratzki, M.: Zur Kenntis der Cerebroflüssigkeit, Ztschr. f. Physiol. Chem. **35**:211, 1902.

added sugar was recovered from the spinal fluid with this method within from 1 to 3 mg. of the calculated amount. Varying amounts of fluid (0.5 c.c., 1 c.c., 2 c.c.) gave identical results.

The Folin method used was a modification of the new Folin sugar method. To 0.2 c.c. of spinal fluid are added 1.8 c.c. of distilled water in a Folin-Wu sugar tube. Then 2 c.c. of Folin's standard are pipetted into another tube. To each are added 2 c.c. of Folin's quantitative copper sulphate solution, and both are heated for six minutes in a boiling water-bath. Then 2 c.c. of molybdate-phosphate are added to each tube; the tubes are cooled, and the solutions diluted to 25 c.c. The standard is set at 20, the comparison made in the colorimeter, and the calculations made as above.

With either of these methods satisfactory results are obtained. Both give practically the same results, but the Folin method is shorter, and when simultaneous blood sugar determinations are to be made the same reagents may be used.

SUGAR IN SPINAL FLUID IN NORMAL PERSONS

There has been considerable divergence of opinion as to the normal amount of sugar to be found in the spinal fluid. Claude Bernard placed the normal amount of sugar in the spinal fluid at 18.8 mg. per 100 cubic centimeter. Kopetski [7] at 46 mg., Mestrezat [1] at from 48 to 53 mg., Schloss and Schroeder [6] at from 54 to 139 mg., Nawratzki [11] at 55.5 mg., Levinson [12] at from 64 to 90 mg., Seham and Nixon at from 64 to 90 mg., and Mott [13] at from 15 to 18 mg.

TABLE 1.—*Normal Spinal Fluid Sugar*

	Hosp. No.	Sugar in Mg. per 100 C.c.	Diagnosis		Hosp. No.	Sugar in Mg. per 100 C.c.	Diagnosis
1	4575	66	Without psychosis	8	4365	53	Psychopathic personality
2	4388	71	Without psychosis	9	4434	58	Psychopathic personality
3	4415	57	Without psychosis	10	4514	64	Psychopathic personality
4	4570	66	Psychoneurosis	11	4450	58	Psychopathic personality
5	4585	63	Psychoneprosis	12	4526	79	Psychopathic personality
6	4402	84	Psychoneurosis	13	4580	68	Psychopathic personality
7	4468	58	Psychoneurosis				

The figures in Table 1 are presented in order that some idea may be obtained as to the normal amount of reducing substance in the spinal fluid. The cases chosen for this purpose showed no physical defects and are usually conceded to have no gross somatic basis, but this does not exclude the possibility that there may be some as yet unknown physical anomaly present. While the number of cases is small, some interesting observations may be made. In this group of cases, the normal spinal fluid sugar ranged between 53 and 84 mg. per 100 cubic centimeters. Most of the determinations fell between 53 and 68 mg. per 100 cubic

12. Levinson, A.: Cerebrospinal Fluid in Health and Disease, St. Louis, The C. V. Mosby Co., 1919.

13. Mott, F. W.: The Cerebrospinal Fluid, Lancet **2**:79, 1910.

centimeters, while three rose above 70 mg. It is probable that the spinal fluid sugar in normal conditions is higher than would be indicated by the literature.

At the present time comparative blood and spinal fluid studies are being made at this hospital on normal, nonhospital subjects, to determine the normal spinal fluid sugar level.

SPINAL FLUID SUGAR IN EPIDEMIC ENCEPHALITIS

The observation by von Economo in 1917 that the sugar of the spinal fluid was increased in this disease was probably the first observation on this matter. After the appearance of epidemic encephalitis in France in 1918, numerous observations were made in which it was claimed that the spinal fluid in epidemic encephalitis held a "high sugar content." Netter,[14] in 1920, reported eight cases in which he showed a sugar content of between 70 and 87 mg. with an average of 86 mg. Laporte and Rouzaud reported twelve cases of epidemic encephalitis with a variation in the sugar content of between 66 and 101 mg. with an average of 88 mg. per 100 cubic centimeters. Marie and Mestrezat [15] report one case with a spinal fluid sugar of 94 mg., and Dopter [16] finds an average of 85 mg. per 100 cubic centimeters of spinal fluid in a series of thirteen cases. Coppe [17] in a series of eleven cases finds a range in the sugar of between 54 and 94 mg., with an average of 74 mg. per 100 cubic centimeters. On the other hand, several observers have found that other conditions besides encephalitis may be responsible for a high spinal fluid sugar. Coppe,[17] for example, found a greatly increased amount of sugar in four cases of syphilitic meningitis, in four cases of epilepsy and almost uniformly in general paresis. In one case of imbecility he found 111 mg. of sugar per cubic millimeter of spinal fluid. He does not believe that the French tendency to regard a high sugar content as characteristic of epidemic encephalitis is justified, "as figures quite as high occur in many other nervous diseases." The statement of the French authors that the sugar content is high is due to the fact that they have used the figures of Mestrezat (from 48 to 53 mg.) for the normal, and have regarded everything above 53 as a high sugar content. Foster [18] in eleven cases of epidemic encephalitis found that the sugar content averaged 76 mg. per 100 cubic centimeters. Stevenson [19] found an

14. Netter: Bull. et mém. Soc. méd. d. hôp. de Paris **44**:103, 1920.

15. Marie, P., and Mestrezat, M.: Acad. de méd. Paris **44**:1246, 1920.

16. Dopter, M.: Bull. acad. de Paris **83**:348, 1920.

17. Coppe, R.: The Sugar Content of the Cerebrospinal Fluid and Its Diagnostic Value, Especially in Encephalitis, Quart. J. Med. **15**:1, 1912.

18. Foster, H. E.: Hyperglycorrhachia in Epidemic Encephalitis, J. A. M. A. **76**:1300 (May 7) 1921.

19. Stevenson, L. D.: A Comparative Study of the Sugar Content of the Spinal Fluid in Diseases of the Nervous System, Arch. Neurol. & Psychiat. **6**:292 (Sept.) 1922.

average of 60 mg. in four cases. It may be seen, therefore, that there is considerable controversy, not only as to whether there is an increase of the spinal fluid sugar in epidemic encephalitis, but also as to whether this is pathognomonic of the disease. Most observers agree at the present time with Dopter [16] and Bénard,[20] who emphasize the fact that the sugar estimation is important as a diagnostic sign, but is not always, although generally, high in epidemic encephalitis. The former considers it of great value in differentiating epidemic encephalitis from tuberculous meningitis.

In all, thirty-five determinations were made at this hospital on thirty-one patients. The series shows a range in the spinal fluid sugar between 52 and 111 mg. per 100 cubic centimeters. The average of the entire series is 82.1 mg. Three determinations were less than 60 mg.; one of these was made over two weeks after the onset of the illness,

TABLE 2.—*Spinal Fluid Sugar in Epidemic Encephalitis*

	Name or Hosp. No.	Sugar in Mg. per 100 C.c.	Day After First Recognized Symptom		Name or Hosp. No.	Sugar in Mg. per 100 C.c.	Day After First Recognized Symptom
1	Gli.	111	3	18	Alt.	52	16
2	Fred.	85	4	19	Tol.	82	6
3	Fred.	86	6	20	4477	85	6
4	Lun.	76	4	21	4366	68	9
5	Lund.	98	4	22	4380	00	8
6	Lock.	62	8	23	4239	77	12
7	Lock.	63	10	24	4557	85	5
8	Lun.	78	6	25	Hard.	91	6
9	Low.	59	12	26	4593	104	4
10	Low.	59	15	27	4882	87	3
11	Eg.	91	3	28	4100	77	8
12	Alt.	94	3	29	2047	63	9
13	Tue.	87	2	30	2068	95	4
14	Wels.	82	3	31		77	6
15	Schu.	87	5	32	3949	74	6
16		77	7	33	2286	90	4
17	Sal.	98	4	34	2628	87	5
				35	2222	77	5

when the patient was much improved; the other two determinations were made on a doubtful case which came to us about twelve days after the onset of the symptoms. If these determinations be discarded, the average reaches 85 mg. per 100 cubic centimeters. Closer analysis of the figures will show that of the thirty-five determinations twenty-five, or 62 per cent., ranged between 76 and 98 mg. Only two determinations rose to 100 or over, and but three fell below 50, while five were between 60 and 75 mg. Examination of the sugar during the first four days of the illness shows an average of 92 mg. per 100 cubic centimeters. Thus, it is evident that the majority of these cases show an increase in the spinal fluid "sugar" according to all standards except those of Schloss and Schroeder.

20. Bénard, E.: Paris méd. **35**:475, 1920.

SPINAL FLUID SUGAR IN MENINGITIS

In the acute cases of meningitis due to the meningococcus, the spinal fluid sugar is either absent or greatly decreased, according to Schloss and Schroeder,[6] Kraus and Corneille,[21] Laroche and Pignot,[22] Kopetzki,[7] and Connall.[8] Hopkins [2] found that the blood sugar was greatly increased and the spinal fluid sugar greatly decreased. He concludes that "it may be possible that the hyper-glycorrhachia which is accompanied by an initial increase is more than offset by the destructive activity of the organism present." He believes that the estimation of sugar is of special importance in differentiating meningitis from meningismus. From the point of view of prognosis, Laroche and Pignot [22] found that the sugar reappears in the spinal fluid in favorable cases on the fourth or fifth day, and disappears or becomes much reduced again as a relapse impends. They say that a low sugar content, persisting low as the disease continues, is an unfavorable sign. Kraus and Corneille [21] showed in several cases that the sugar content rose in a patient who recovered and fell in one who died. They not only consider this decrease to be of prognostic significance, but state that it disputes the statement that in the acute stages the sugar is absent and reappears only with recovery. Hopkins [2] considers the sugar test to be of value in prognosis, as he found an increase in sugar with a decrease in the number and virulence of the bacteria. Sicard and Rousseau, Mestrezat,[1] Jacob and others also believe the sign is of prognostic value.

TUBERCULOUS MENINGITIS

This disease is considered separately because the spinal fluid sugar determinations are different in many ways from those of the acute meningitides. Schloss and Schroeder [6] analyzed twenty-three cases of tuberculous meningitis and found that the sugar was either normal, slightly decreased or greatly decreased. They could ascribe this variation to no definite influence. They found, however, a definite decrease at some stage and considered only a decrease to be of diagnostic importance. Connall [8] analyzed 122 cases and found sugar present in the great majority at all stages of the disease, but greatly decreased. He found complete absence in only two cases. Hopkins [2] found an average of 35 mg. per 100 cubic centimeters in twenty cases of tuberculous meningitis. In two of these the figures were normal. Rieger and Solomon [4] report one case with a sugar content of 26 mg. per 100 cubic centimeters. Coppe [17] reports twelve cases which average 28 mg. per

21. Kraus, W. M., and Corneille, G. C.: The Sugar Content of the Cerebrospinal Fluid in Health and Diseases, J. Lab. & Clin. Med. **1**:685, 1916.

22. Laroche, A., and Pignot, J.: The Sugar in the Spinal Fluid in Acute Meningitis, Paris méd. **7**:293, 1917. Pignot, J.: The Sugar Content of the Spinal Fluid, ibid. **8**:321, 1918.

100 cubic centimeters, and concludes that "an investigation of the sugar in the spinal fluid by a quantitative method is especially valuable in tuberculous meningitis." Leopold and Bernhard [23] found figures of 40, 50 and 80, in three cases of tuberculous meningitis. One may safely conclude, therefore, that in a tuberculous meningitis the sugar of the spinal fluid is greatly decreased. It may be normal in a few cases, but it usually ranges between 25 and 35 mg. per 100 cubic centimeters.

Only three determinations on the spinal fluid sugar in tuberculous meningitis were made in this hospital. Of these, one showed a sugar content of 70 and a paretic curve with Lange's colloidal gold test; the other two showed 35 and 31 mg. of sugar per 100 cubic centimeters of spinal fluid.

SPINAL FLUID SUGAR IN GENERAL PARESIS

Mestrezat,[1] in 1912, concluded that the sugar of the spinal fluid is uniformly increased in untreated general paresis. This finding was later confirmed by Mott, who found very high figures. Weston [24] found

TABLE 3.—*Spinal Fluid Sugar in General Paresis—Untreated*

	Name or Hosp. No.	Sugar in Mg. per 100 C.c.		Name or Hosp. No.	Sugar in Mg. per 100 C.c.
1	Abr.	76	14	Cobe.	90
2	Mil.	75	15	Lys.	65
3	Rel.	63	16	McLan.	46
4	Nas.	61	17	4629.	48
5	Mun.	74	18	1427.	40
6	Ter.	87	19	2565.	76
7	Cps.	86	20	4420.	65
8	And.	46	21	4000.	49
9	Pec.	72	22	4429.	75
10	Pul.	60	23	4413.	56
11	Publ.	62	24	4409.	81
12	Sana.	83	25	Luth.	72
13	Whe.	52			

an average sugar content of 71.8 mg. in twenty cases of untreated paresis, as against an average sugar of 72.5 mg. in nine cases of treated paresis. Rieger and Solomon [4] state that they were unable to confirm the fact that the sugar is increased in untreated paresis. Kaplan [8] found the sugar in untreated paresis to be increased, while in cerebrospinal syphilis he found it to be low. Biach, Kerl, and Kabler [25] found the sugar in fourteen cases of untreated paresis to range between 40 and 90 mg., while in twelve cases of syphilis (in which the type is not stated) there was a marked *rise* in the sugar one case reaching 340 mg. Turner,[9] using Fehling's quantitative test, found an average sugar of

23. Leopold, S., and Bernhard, A.: Studies in the Chemistry of the Spinal Fluid of Children, Am. J. Dis. Child. **13**:34, 1917.

24. Weston, Paul: The Sugar Content of the Blood and Spinal Fluid of Insane Subjects, J. M. Res. **35**:199, 1916.

25. Kabler, H.: The Sugar Content of the Spinal Fluid in Internal Diseases and Nervous Affections, Wien. Klin. Wchnschr. **35**:8, 1922.

16.75 mg. in seven cases of paresis. He does not specify whether the patients were treated or untreated. In one case of paresis he found no sugar. Coppe [17] found the sugar approximately normal in ten cases of paresis. Karpas [26] says the sugar is not increased in untreated paresis.

In twenty-five cases of untreated paresis at this hospital the variation in the spinal fluid sugar was between 40 and 90 mg. The general average was 65 mg. per 100 cubic centimeters. It is noteworthy that in a certain proportion of our series of cases of untreated paresis the spinal fluid sugar is present in amounts quite as high as in epidemic encephalitis.

TABLE 4.—*Spinal Fluid Sugar in General Paresis—Treated*

	Name or Hosp. No.	Sugar in Mg. per 100 C.c.		Name or Hosp. No.	Sugar in Mg. per 100 C.c.
1	Sor.	56	21	Good.	59
2	Rus.	42	22	Be.	52
3	Reins.	47	23	Les.	69
4	Con.	61	24	Rus.	61
5	Kear.	52	25	Con.	59
6	Gold.	59	26	McD.	69
7	Mat.	53	27	Sor.	88
8	Lus.	45	28	Le.	59
9	McD.	43	29	Pec.	59
10	Con.	86	30	Rus.	42
11	Gul.	65	31	Hub.	51
12	Gol.	57	32	Stev.	65
13	Beat.	65	33	Pal.	61
14	McD.	51	34	727.	50
15	Lus.	49	35	4151.	56
16	McD.	50	36	1505.	61
17	Con.	59	37	3911.	52
18	Sor.	50	38	2205.	47
19	Good.	50	39	2841.	43
20	Be.	52			

SPINAL FLUID SUGAR IN GENERAL PARESIS—TREATED

In our series we have forty cases of treated general paresis. Many other determinations were made on fluids from this series, but they are not included here because they are merely repetitions of the determinations in a great many cases. The variation in the sugar content in this series is from 42 to 88 mg. per 100 cubic centimeters. The average for the series of cases of treated paresis is 55.4 mg. .The latter figure is entirely within normal limits, but when compared with that of untreated paresis, one finds that it averages about 10 mg. below the former figure, a change that is of little significance.

SPINAL FLUID SUGAR IN DEMENTIA PRAECOX

Turner found an average sugar of 20.3 mg. in nine cases of dementia praecox. Weston [24] found an average sugar content of 60.4 mg. in twenty cases of dementia praecox.

26. Karpas, M. J.: The Clinical Interpretations of the Serological Content of the Blood and Cerebrospinal Fluid, with Some Reference to the Cytology and Chemistry of the Latter in Mental Diseases, Am. J. Insan. **69**:134, 1912.

TABLE 5.—*Spinal Fluid Sugar in Dementia Praecox*

	Hospital Number	Sugar in Mg. Per 100 C.c.		Hospital Number	Sugar in Mg. per 100 C.c.
1	4341	58	12	4470	78
2	4347	88	13	4486	54
3	8049	123	14	4467	58
4	3464	80	15	4500	85
5	4416	66	16	4521	58
6	4410	72	17	4512	81
7	4399	71	18	4582	103
8	4357	60	19	4611	83
9	4461	65	20	4608	84
10	4441	68	21	4513	76
11	4471	73			

In twenty-one cases of dementia praecox which were examined at this hospital the average spinal fluid sugar was found to be 80.1 mg. It should be noted that the number of determinations over 70 or 80 mg. per 100 cubic centimeters are considerable in this series, *so that in dementia praecox we have another condition that may give a sugar content fully as high as in encephalitis.*

SPINAL FLUID SUGAR IN MANIC-DEPRESSIVE PSYCHOSIS

Eleven fluids were examined from cases of manic-depressive psychosis. The average spinal fluid sugar was found to be 66.9 mg. In manic-depressive insanity, in contrast to the findings in dementia praecox, the sugar in the spinal fluid is essentially normal.

TABLE 6.—*Spinal Fluid Sugar in Manic-Depressive Insanity*

	Hospital Number	Sugar in Mg. per 100 C.c.	Phase		Hospital Number	Sugar in Mg. per 100 C.c.	Phase
1	4426	66	M. D. Depressed	6	4439	70	M. D. Manic
2	4398	71	M. D. Manic	7	4480	60	M. D. Depressed
3	4535	77	M. D. Depressed	8	4506	68	M. D. Depressed
4	4339	60	M. D. Mixed	9	4508	72	M. D. Depressed
5	4411	82	M. D. Depressed	10	4569	51	M. D. Hypomanic

The figures in Table 7 are worthy of particular mention. In the first place, the figures for diabetes mellitus show a greatly increased

TABLE 7.—*Spinal Fluid Sugar in Miscellaneous Conditions*

Name or Hosp. No.	Sugar in Mg. per 100 C.c.	Diagnosis	Name or Hosp. No.	Sugar in Mg. per 100 C.c.	Diagnosis
....	140	Paralysis agitans	4578	76	Involutional melancholia
4457	56	Alcoholic psychosis	4507	76	Involutional melancholia
4414	79	Alcoholic psychosis	....	75	Multiple sclerosis
4516	68	Cerebral arteriosclerosis	....	73	Postinfluenzal psychosis
....	60	Cerebral arteriosclerosis	....	82	Puerperal delirium
....	82	Cerebral embolism	4419	68	Senile psychosis
....	100	Cerebral embolism	4501	68	Senile psychosis
....	125	Cerebral thrombosis	4571	68	Senile psychosis
4361	69	Cord lesion	4449	67	Organic brain disease
Au	123	Diabetes mellitus	4423	64	Toxic delirium
Cur	180	Diabetes mellitus	4362	61	Sydenham's chorea
4455	68	Involutional melancholia	....	77	Undiagnosed
4376	72	Involutional melancholia	4325	68	Undiagnosed

spinal fluid sugar. The blood in these cases gave readings of 326 mg. and 430 mg. per 100 cubic centimeters, respectively. Very high figures were found in the spinal fluid in cases of cerebral embolism, thrombosis and paralysis agitans. Indeed, in other conditions such as we had, results were obtained which were well above the supposed limits of normal, *so that here, too, are numerous conditions which give at times spinal fluid sugars fully as high as in epidemic encephalitis, but not so constantly as in the latter condition.*

SUMMARY AND CONCLUSIONS

1. A study of 421 spinal fluid sugars is presented, representing determinations in the normal person, in epidemic encephalitis, in general paresis (treated and untreated), in dementia praecox, in manic-depressive insanity and in various miscellaneous conditions.

2. The figures for the normal spinal fluid sugar represent the results of determinations on thirteen presumably normal persons. The normal range was found to be from 50 to 65 mg. per 100 cubic centimeters of spinal fluid. This agrees with the observations of Nawratzki, Seham and Nixon, and Levinson.

3. The sugar in epidemic encephalitis is generally increased. Observations in thirty-five cases place the average figure at 82 mg. per 100 cubic centimeters, the mean average being 84.5 mg. per 100 cubic centimeters. Our conclusion is that the test is not pathognomonic, but is of distinct diagnostic value. Other conditions give a high spinal fluid sugar. Our figures agree with those of Netter, Marie, Mestrezat and Dopter, and are somewhat higher than those reported by Foster.

4. The spinal fluid sugar in untreated general paresis is not increased. A series of twenty-five cases shows an average of 65 mg. per 100 cubic centimeters. Several of these cases, however, showed an increase in sugar fully as high as in epidemic encephalitis. Our findings corroborate those of Weston, Rieger, Solomon and Coppe, who found no increase in the sugar in untreated paresis.

5. The spinal fluid sugar in cases of treated general paresis averages 55.4 mg. per 100 cubic centimeters in 163 cases. This is entirely within normal limits, but lower than in the untreated cases.

6. The spinal fluid sugar in twenty-one cases of dementia praecox shows an average of 80.1 mg. per 100 cubic centimeters. One case showed a sugar of 103 mg. and another 123 mg. per 100 cubic centimeters. Twelve fluids showed a sugar content between 70 and 80 mg. per 100 cubic centimeters, so that cases of dementia praecox may give sugar values fully as high as in epidemic encephalitis, though not as frequently.

7. The spinal fluid sugar in manic-depressive insanity is normal. Eleven cases of this disorder gave an average sugar of 66.9 mg. per 100 cubic centimeters.

8. Two cases of diabetes mellitus showed spinal fluid sugars of 123 and 189 mg. per 100 cubic centimeters.

9. The Benedict-Osterberg method for urine as modified by us for spinal fluid was used. This was controlled in each case by a determination by the Folin-Wu sugar method.

THE RELATION BETWEEN INFANTILE CONVULSIONS AND THE CHRONIC CONVULSIVE DISORDERS OF LATER LIFE*

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This report is the initial step in what is to be an extended study. The problem is to determine not only the relation between infantile convulsions and the chronic convulsive disorders of later life, but also to ascertain which type of convulsions may be considered malignant and which, if any, may be called benign. The attitude of the general practitioner and even of the pediatrician, toward infantile convulsions, is familiar. The convulsions ordinarily are minimized, even to the extent of being reduced in importance to that of a rise in temperature.

In a group of 300 cases taken at random at the Monson State Hospital for Epileptics, in which the information was sufficiently detailed and authenticated to be thought worthy of consideration, 150 patients had their first convulsion prior to the fourth year. I am not sure that this percentage is not a bit high, and that a larger group of cases would perhaps show some slight difference. However, the fact remains that childhood is the most important period for the study of convulsive disorders.

The records at the Massachusetts General and at the Infants' and Children's Hospitals have been at my disposal, and in order to get a representative group of the convulsive disorders of infancy, the problem was approached in a different way at each hospital. At the Massachusetts General Hospital, we read the records in all cases in which there was a history—first, of general convulsions; and second, of rickets, spasmophilia, tetany and whooping cough in children under 4 years of age. Six hundred and ninety-one records were studied, covering the period between 1903 and 1922. At the Infants' Hospital the records of all admissions (1,153) for the years 1915 and 1916 were studied and at the Children's Hospital the records of sixty-three patients, in whom a diagnosis of convulsions, spasmophilia or tetany had been made, were investigated.

From the Infants' and Children's Hospitals I was able to get a group of cases in which the convulsions might be considered incidental; i. e., the patient did not necessarily go to the hospital because of the convul-

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* Read before the Association for Research in Nervous and Mental Diseases, New York, December, 1922.

sions. In none of these cases had a diagnosis of epilepsy been made, the convulsions usually being considered incidental to an acute infection, gastrointestinal upset, rickets, etc.

I have collected from the three hospitals mentioned 111 patients who had convulsions prior to the fourth year, not associated with any acute or chronic cerebral condition, such as encephalitic and meningitic processes, neoplasms, and other conditions due to lack of cerebral development. All cases in which there was any evidence of birth trauma, or other brain damage manifested by neurological signs and symptoms, were eliminated. The cases considered were those in which the convulsions were associated with gastro-intestinal disturbances, acute infections, spasmophilia, pertussis, rickets, and also eleven cases in which there was no associated disease or symptom complex, other than the convulsions. This group, small as it may be, represents the type of convulsion that causes little anxiety either to the physician or parent. The importance of this sort of convulsion as an indication of instability of the nervous system has perhaps been overlooked. It is, however, too early to emphasize this point. Let us first investigate the subsequent history of these patients.

For this preliminary study, the 111 cases have naturally divided themselves—according to the subsequent findings—into two groups; the first with probable brain damage and the second without evidence of brain damage. The accompanying table presents many points of interest.

Summary of 111 Children with Convulsions Occurring Before the Fourth Year, and Subsequent Medical History

Malignant Group

	Convulsions Continued Until Death	Epileptic	Mentally Deficient	Total
First convulsion associated with:				
Gastro-intestinal upset	4	15	5	24
Acute infection	4	4	2	10
Spasmophilia	9	2	5	16
Pertussis	0	0	0	0
Rickets	1	3	2	6
Unknown Cause	1	4	1	6
	19	28	15	62

Benign Group

	Not Strong	Well	Total
First convulsion associated with:			
Gastro-intestinal upset	7	11	18
Acute infection	4	8	12
Spasmophilia	4	9	13
Pertussis	1	0	1
Rickets	0	0	0
Unknown Cause	3	2	5
	19	30	49

In the malignant group, I have included all cases in which the convulsions persisted until the time of death, and the living patients who are either having convulsions at the present time, or who are mentally deficient. The children who have survived without evidence of brain damage will not be considered in groups, except to say that seventeen of these cases, although considered mentally normal, are quite definitely below par physically.

It is surprising to find that sixty-two cases, or 56 per cent. of the total number studied, belong in the malignant group, while forty-seven, or 44 per cent. belong to the second group. It is equally striking to learn that twenty-four of the forty-two patients having convulsions associated with gastro-intestinal upsets belong to the brain damage group, of which four are dead, fifteen are living and having convulsions, and five are mentally deficient.

Of the twenty-nine cases in which a diagnosis of spasmophilia was made, sixteen belong to the malignant group. It hardly seems necessary to discuss the subdivisions of the group at this time, as more intensive study of each case will be required before we are justified in drawing conclusions. There are certain points, however, that seem of sufficient interest to mention in passing. For example, of 400 cases of whooping cough, in only six were we able to obtain a history of convulsions during their hospital stay.

There seems to be no uniformity of opinion regarding the frequency of infantile convulsions, and work is now being done to determine this point with some degree of accuracy. At the Children's Hospital, in the year 1919, there were 5,408 admissions; the diagnosis of convulsions was made twenty-three times, and that of spasmophilia forty-three times, indicating that in that particular group, at least, convulsions occurred only a little more frequently than once in every one hundred cases. In another large series of records read, convulsions occurred prior to the fourth year in one case in every forty-six. This is undoubtedly a very low percentage.

The only contribution * with which I am familiar, that is similar to the one I am presenting, was made by Dr. John Lovett Morse, at the thirty-first annual meeting of the American Pediatric Society, in June, 1919, and it is of particular interest to those of us who are primarily concerned with the nervous system that it came from a pediatrician. The following is a summary of Dr. Morse's paper:

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* Doctors Hugh T. Patrick and David M. Levy reported before the Chicago Neurological Society their results of a most interesting and valuable study, "Early Convulsions in Epileptics and in Others." A summary of this report was printed in the December number of the Archives of Neurology and Psychiatry and the article appeared in full in the Journal of The American Medical Association.

Dr. Morse definitely shows that thirty-nine of his cases are considered abnormal. I am not quite sure, however, of the mental status of the remaining sixty-eight cases, and it is unlikely that, from a neuropsychiatric point of view, all these cases would be considered normal. Assuming for statistical purposes that these sixty-eight cases were normal, and combining the two groups (Dr. Morse's and my own), we find that 101, out of a total of 218 patients having infantile convulsions, are definitely abnormal—a fact which is sufficiently striking and contrary to our present-day conception of infantile convulsions to justify further study.

There are two or three questions that immediately arise in the mind of one working on a problem of this sort. The first is: How does the material utilized in this particular study, representing largely hospital cases, compare with the material that one would find in private practice? That is, does the convulsive group of cases that goes into the hospitals represent perhaps a more malignant or serious type of case than one would find in private practice? Perhaps the family background in the hospital group represents a more unstable stratum of society. Then, too, we are dealing with a rather selected group of cases that does not fairly represent the community as a whole. At this time I cannot answer this question.

Further, the question of diagnosis is one that always arises in a discussion of any group of cases when we are not absolutely certain of the means and methods utilized in reaching the conclusion presented. The diagnoses in this group of cases were made in three hospitals where medical standards are above the average. In the cases of spasmophilia, for example, although the electrical reactions and determination of calcium content may not have been carried out in all cases, the symptom complex presented what is generally being termed spasmophilia by the medical profession. A similar line of reasoning holds true for the diagnoses of other groups of cases. In discussing this problem with pediatricians, one is immediately impressed with the fact that in a very large percentage of cases, their contact lasts only a comparatively short time. Consequently, it would not be surprising to find that the events following convulsions in children are more serious than the pediatrician would lead us to believe. As neurologists and psychiatrists, we appreciate how difficult it is to determine in adult life what actually happened during the period of childhood, especially when dealing with patients in families in which there have been several children.

Notwithstanding the fact that meningitic and encephalitic cases were not considered in this study, my attention was called to two cases of cerebral meningitis associated with convulsions, occurring in children under 4, who are now over 12 years of age. These children may now be considered perfectly normal and healthy: they are both doing well

in school and have had no convulsions since the meningitic process subsided.

It occurs to me that the type of nervous system that reacts with convulsions in the presence of some mild toxemia associated with gastrointestinal upsets, is perhaps the type of nervous system that needs protection from environmental situations. By that, I mean that the individual must be steered so as to avoid many of the gales which the normal individual is quite capable of weathering. For instance, the two patients in the meningitic group who reacted to this rather severe storm with convulsions. When the meningitic process subsided, the convulsions ceased and the individuals were able to carry on quite well without any evidence of brain damage. Thus the convulsions may perhaps be considered as the criterion of the stability or instability of the nervous system. Childhood offers a better opportunity to study the physiologic, biologic, and biochemical aspects of the individual than any other period.

A METHOD OF DETERMINING THE MENTAL AGE DURING A PHYSICAL EXAMINATION *

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Before his examination is finished, the physician has usually formed an opinion about his patient's intelligence. For this opinion he has many guides. He may observe the speed and skill with which his commands are carried out. He may note the judgment, precision, and information shown in answer to his routine questions. He may observe his patient dressing and undressing, lying on a table, weighing on a scale, reading letters from a vision chart, and many other performances, that have to do with intelligence. Moreover, these responses are made in a very natural way. The patient has no consciousness of being tested as in the mental testing room. The examining physician gets ready cooperation and in this respect has a real advantage. This is especially true of those older delinquent children who are resentful of "tests," yet quite willing to take the physical examination.

The physical examination affords opportunities for many observations other than those concerned primarily with physical disease. The psychiatrist especially has learned to take advantage of this. The peculiar gestures of the patient, his queer manner of handling his clothes, of sitting down or of lying on the examining table; his variations in the manner of responding to simple commands performed in a very standard way—all such observations influence the psychiatrist's judgment of the patient's intelligence, personality and mental status. Such evidence is not usually evaluated properly. More often it probably represents the stuff out of which clinical "hunches" are derived, or such formulations as "well, I feel sure that this patient is feebleminded or psychotic" (etc.); "there is something in his manner or in his way of doing things."

An attempt to evaluate such observations was started in January, 1920, at the Illinois Institute for Juvenile Research. These observations comprised a long list of which the following are samples: (1) dressing and undressing; (2) position on chair and table; (3) information as to name, age, height, weight; (4) memory of height and weight after these were determined and told to the patient; (5) ability to find the correct weight on a standard type of scales, after instruction, if necessary; (6) behavior during the one minute Romberg test; (7) reactions to suggestions of hyperesthesia and hypesthesia; (8) responses to cer-

* From the Illinois Institute for Juvenile Research.

tain commands. During their collection, these data were compared with the findings of the psychiatrist, the mental tester, and the social historian. It was soon found empirically that certain of them had high correlative value, some had value in themselves, but that most of them had too little or indeterminate value for practical purposes.

This paper is the first record of this investigation. It is a selection of certain directions given patients during the physical examination, which were found to have an unusually high correlation with the Stanford-Binet mental age scores between the years five and eleven.[1] After a standard procedure and method of scoring were developed, several psychologists were taught the technic. I am especially indebted to Miss Phyllis Bartelme and Miss Elizabeth Lord of the psychologic staff of the institute. The results presented are based largely on data accumulated by them and by the author.

Four hundred and twenty-six cases have been used in the tests. The cases represent a miscellaneous group from the Institute for Juvenile Research, the Lincoln State School and Colony (for feeble-minded), and the Cook County Juvenile Detention Home, Chicago. The diversity of types is an advantage in that the weakness of tests supplementary to the Stanford-Binet is especially brought out by patients whose responses to the standard series is characterized by much scattering as compared with a normal group.

The tests are unusually brief—three to four minutes for the series. They consist of a standardized form of directions for the finger-to-nose, finger-to-finger, and knee-to-heel coordination; for spreading out the fingers of both hands and reading the letters from the visual chart with a card placed over one eye. These tests are not a substitute for any standardized revision of the Binet-Simon tests. They give the physician an approximate estimate, however, that is sufficient to indicate the need of further tests. Sometimes in the case of adults the tests may be applied when there is not sufficient cooperation for the longer Stanford-Binet examination.[2]

In practice I have found the tests of value especially in the following circumstances:

1. In checking the Stanford-Binet mental age in cases showing very irregular attention, when, however, cooperation during briefer tests

1. $r = 0.943$ (Pearson); P.E. $= 0.002$; regression coefficients: $b_1 = 98.7$, $b_2 = 89.0$.

2. In this paper, only the directions for giving the test and determining the mental age are presented, without considering such problems as the method of selecting the type of observation used, the reason for the high correlation, and the relation of these observations to habits, abnormal behavior, and findings other than intelligence.

could be secured, especially in schizophrenics and postencephalitic children.

2. Examining prisoners through the bars, where no other access was allowed.

3. As an elimination test for the Stanford-Binet examination in the case of adults when pressed for time (as in prison).

4. Cases resisting mental tests, especially in egocentric psychopaths; also in office practice when for some reason or other it was not considered practical to give a formal test. When given during a physical examination, the patient does not know he is being mentally tested.

Scores

Combination	Test 1, FN (Finger-nose)	Test 2, FF (Finger-finger)	Test 3, KH (Knee-heel)	Mental Age
1	0	0, ap.	0	From less than 5 to $5^{5}/_{12}$ yrs.
2	+	0	0	From 5 to $5^{11}/_{12}$ years
3	+	ap., 0+	0	From 6 to $6^{5}/_{12}$ years
4	+	0, ap., 0+	0+	From 6 to $6^{11}/_{12}$ years
5	+	0, ap., 0+	+	From 7 to $7^{5}/_{12}$ years
6	+	+	0, 0+	From 7 to $7^{5}/_{12}$ years
7	+	+	+	From 7½ to $7^{11}/_{12}$ years

Combination	Test 4, Ch (Chart)	Test 5, SOF (Spread-out-fingers)	Mental Age
1	1	2	From 8 to $8^{5}/_{12}$ years
2	2	1	
3	1	3	From 8½ to $8^{11}/_{12}$ years
4	2	2	
5	3	1	From 9 to $9^{5}/_{12}$ years
6	1	4	
7	4	2	
8	4	1	From 9½ to $9^{11}/_{12}$ years
9	2	3	
10	2	4	
11	3	3	From 10 to $10^{5}/_{12}$ years
12	4	3	
13	4	2	
14	3	4	More than 10½ years
15	4	4	More than 11 years

DIRECTIONS FOR GIVING TESTS

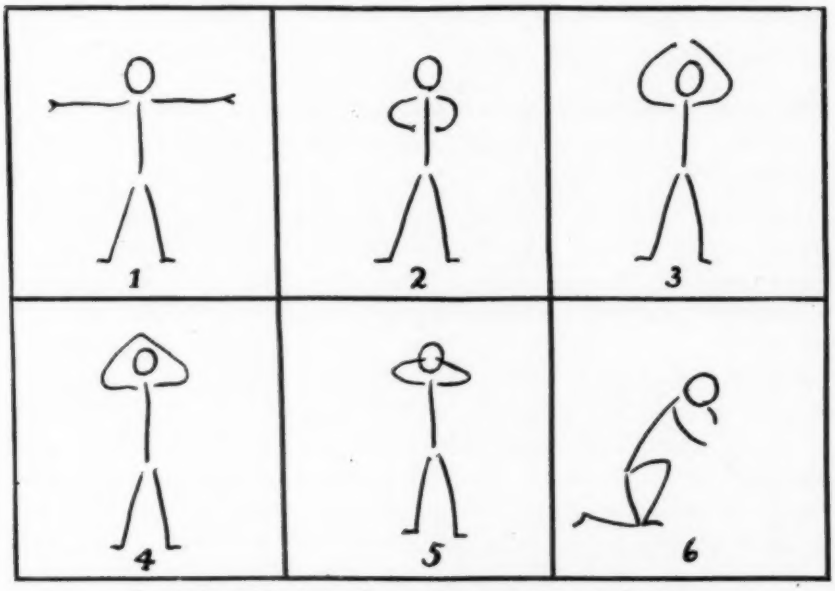
It is best to stand facing the patient, who also stands throughout the tests. The directions should not be read to the patient. While learning the test, read each direction separately to yourself until you can say it without referring to the printed sheet. Speak slowly and clearly, with emphasis. The standards are based on the directions as printed and a variation of one word, even though it may improve the form of expression, throws out the score. In case of a physical difficulty, it is easy to decide whether the patient fails because of intelligence or because of the physical handicap; for example, when the finger-to-finger directions are performed as directed, but because of incoordination the fingers are not brought together. Written records should be made

at once. As will be seen from the directions on the scores, close observation is necessary. Although the matter of scoring appears difficult, it is in reality simple, as a few trials will show. The patient may be dressed or undressed. The test may be given for its own value without a physical examination.

TECHNIC OF TESTS

Introduction.—"I am going to tell you to do a number of things. You must listen carefully. Now, are you ready?" (Be sure you have the patient's attention.)

TEST 1.—F. N. (two trials): "Close your eyes and touch the tip of your nose with the tip of your finger."



Symbols to illustrate the various responses to the tests.

TEST 2.—F. F. (two trials): "Spread your arms way out to the sides and then bring the tips of these two fingers together way in front of you with your eyes closed." (Hold your index fingers in front of you, about 6 inches apart on a level with your face, while saying, "the tips of these two fingers.")

TEST 3.—K. H. (two trials): "Close your eyes and put your left (or right) heel on your right (or left) knee."

TEST 4.—Chart (two trials): "All right. That's very good. Now take this card and go to the wall; with your back to the wall (or window) put the card over your left eye and read aloud the top letter on that chart." (Point to the wall and after giving the card to the patient point to the chart.)

TEST 5.—S. O. F. (two trials): "Now listen to this carefully; it is the last direction; you have done the others very well. Do you know what the palms are? (If the patient does not know, designate them.) Put your hands way out in front of you, palms downward; then spread out your fingers far apart and turn them around until they are palms upward; then stick out your tongue."

DIRECTIONS FOR SCORING

TEST 1, F. N. (finger-nose).—Any success in two trials scores +.

TEST 2, F. F. (finger-finger).—(1) No response or merely spreading the arms as illustrated in Symbol 1 on the accompanying diagram—score 0.

(2) Approximation in front or overhead, as illustrated in Symbols 2 and 3, with fingers touching overhead as in Symbol 4, or touching both eyes or parts of the face, as in Symbol 5, or a failure and a plus—are all partial credits and designated *ap.* (approximation) or 0 +. All fingers together, hooked or touching, scores *ap.*

(3) If two finger tips are brought together, whether index, middle or other, regardless of whether close to or far from the body, high or low, but not overhead — score +.

TEST 3, K. H. (knee-heel).—(1) Failure on first trial, success on second = 0 +.

(2) When directions are followed correctly excepting that right is taken for left or vice versa, score +. Heel to knee in any way is +; e. g. as illustrated in Symbol 6.

TEST 4, (reading chart).—(1) Failure in or omission of two directions — score 1.

(2) Failure in one of the three following directions, but correct on the others — score 2: (*a*) Belly instead of back to wall. Backing to the wall rather than walking or turning, even if not close to the wall, is accepted as correct. (*b*) Card not placed over the eye, or placed over both eyes. It must be at least over one eye. (*c*) Failure to read.

With a score of 1 on the first and 2 on the second trial, score 2. With a score of 1 on the first and 3 on the second trial, score 2.

(3) Score 3 with one of the following failures: (*a*) Card over the wrong eye. (*b*) Reading more than the designated letter or the wrong letter. It is accepted as correct if the patient does not read but says "I can't see." (*c*) Score 3 if directions are all correctly followed but in wrong order. Score 3 if directions are followed but extra movements occur.

Score of 1 on the first with 4 on the second trial = 3; score of 2 on the first and 4 on the second trial, = 3.

(4) Complete success scores 4. If the patient asks for a repetition and then scores a complete success, he is credited 4.

TEST 5, (S. O. F.) (spread-out-fingers).—(1) Failure by omission of two directions — score 1.

(2) Failure on the first trial, with a score of 3 on the second — Score 2.

(3) Score 3 with one of the following three omissions, the other directions being carried out correctly: (*a*) failure to rotate palms; (*b*) failure to spread out fingers; (*c*) failure to put hands "in front."

Score of 1 on the first trial and of 4 on the second = 3.

(4) Score 4 with complete success, or even if the palms are not directed downward, or there is failure to stick out the tongue, or the directions are all followed but in wrong order, or if all are followed but with extra movements, e. g. hands to sides then front, rotation of palms and also turning body around on feet.

Special Note.—When full or partial success occurs on either of Tests 4 or 5 (*a*, 2, 3, or 4) score as if the scores for the first three tests were all plus.

A CASE OF FAMILY PERIODIC PARALYSIS*

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AND
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One of us (C. F. R.) came to the office of the other for diagnosis and treatment. The case record follows.

REPORT OF CASE

History.—On May 11, 1923, a medical student, a man, aged 23, single, complained of a feeling of fulness in both ears for five months, a "queer feeling" for nine months in both sides of the face like contraction of muscles but without visible contraction, and an occasional feeling like electricity on the tongue or as if the tongue had been burned by hot soup. He also had occasional attacks of paralysis of various muscle groups. So far as he could remember, these began at about 12 years of age and had recurred at irregular intervals of weeks to months ever since. On rising after sitting for a long time some muscle would be very weak. Sometimes he developed "toe-drop" or "heel-drop" on one side, both legs never being affected at the same time. On several occasions he had found it impossible to extend the middle finger of the right hand. Sometimes the distal half of an arm or leg seemed to be generally affected, but there had never been complete paralysis of a single limb. These effects lasted for hours or days. They were often preceded by a feeling of soreness, but were never accompanied by any real pain. No vasomotor changes had been noted. Attacks in the last few years had become gradually less frequent, but one foot had been partially paralyzed during the past week. He knew of no special influence or circumstance that brought on an attack involving real paralysis. He had tried not to be introspective about these symptoms, but they were beginning to worry him.

He used tea, coffee, alcohol and tobacco in moderation; he took no drugs, and had a good appetite and normal alimentary functions. Nocturia occurred once regularly. There was no known sexual abnormality. He slept for eight or nine hours and could not work well on less. He was a student and did not have much physical exertion.

He had had whooping cough at the age of 5, measles at 7 and appendectomy with elevation and attachment of the cecum had been performed at the age of 12. Several attacks of malaria had occurred since childhood. At 17 he began to have hay-fever.

The patient was the only child. His paternal great-grandmother is said to have had "rheumatic" attacks which, in the light of later developments, probably were periodic paralysis. One of her daughters had a daughter who developed definite attacks of partial paralysis. Her other daughter, the patient's grandmother, had similar attacks. She had seven children. The oldest had a

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*Read before the Chicago Neurological Society, Jan. 17, 1924.

doubtful case, having suffered from stumbling and weakness ever since an acute fever at the age of 6, when he was overdosed with cathartics. The second, the father of the patient, had had attacks beginning at puberty and recurring every few weeks for some years while he was doing hard physical work. These became less frequent when he began to lead a more sedentary existence. Attacks would come most often in the legs but sometimes in one arm and one leg or in any combination. There had been a steady decrease in frequency until now at the age of 59 he had been having only about one attack a year. His sister, next to him in age, had had similar attacks when she was young. The next four children were free from this trouble. So far, nothing had developed in any of the fourth generation except in the patient (see chart).

General Examination.—The patient weighed 115 pounds (52.16 kg.), was of medium height and slight build. His skin and mucous membranes were of good color. The teeth, tongue, tonsils and thyroid were negative. There were no palpable lymph nodes. The abdomen was negative except for a right rectus

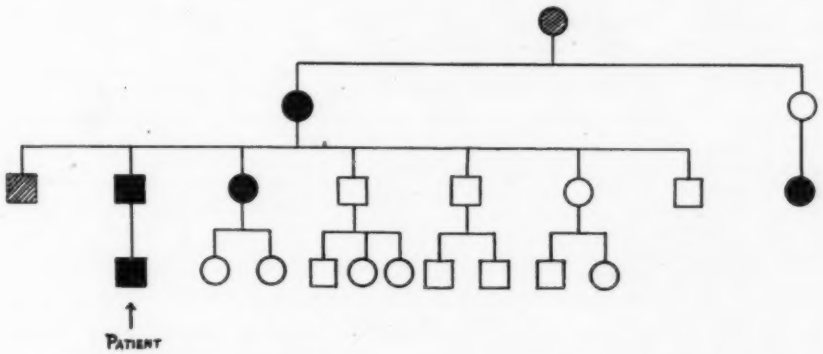

Chart indicating hereditary features. The squares indicate males, the circles females; the black figures, definite cases; the shaded ones, probable cases.

scar. The spleen and kidneys were not palpable. The lungs, heart and vessels were negative. The blood pressure was: systolic, 124, diastolic, 78.

Neurologic Examination.—The motor system, including the gait, coordination, skilled acts, muscle strength, muscle status and nerve status, was entirely normal. There was no abnormal attitude or deformity and no abnormal involutary or associated movements. The following reflexes were normal: biceps, radial, triceps, patellar, Achilles, abdominal, cremasteric and plantar (flexion). Sensation of pain and touch was normal. All the cranial nerves were normal. There was no mental disturbance.

A tentative diagnosis of family periodic paralysis was made.

Course of Illness.—May 12: The Wassermann test of the blood was negative.

May 15: Blood examination revealed: red cells, 5,400,000; white cells, 9,900; hemoglobin, 106. The differential count showed no abnormality. The red cells appeared to be normal. The coagulation time was five minutes.

Examination of a twenty-four hour urine showed: amount, 1,800 c.c.; acidity, 56; specific gravity, 1.022; total solids, 5.12 per cent.; urea, 1.8 per cent.; ammonia, 0.08 per cent. There were no albumin, sugar, indican, diacetic acid or acetone. The sediment was negative.

August 16: In the morning an attack of paralysis developed in the right foot. Office examination in the afternoon showed that the power of dorsal flexion was entirely lost and plantar flexion was very weak. The knee jerks were equal. The left Achilles reflex was present, the right absent; there was no Babinski sign. Electrical stimulation with strong faradic current brought no response when applied to the right peroneal nerve or to the motor points for the right extensor longus hallucis and tibialis anticus. The same stimuli produced lively responses on the left.

August 17: The attack progressed, involving both legs from the knee down although more nearly complete on the right. There was some weakness of the thighs.

August 18: The patient awoke in good condition.

Table 1 is a comparison of the twenty-four hour urine collected during this attack with one taken some weeks later during a normal period. The same diet was used in each instance.

TABLE 1.—*Comparison of Urine During an Attack of Paralysis with That Collected When Patient was Normal*

	Aug. 17	Oct. 12
Amount	800	1,375
Acidity	23	16
Specific gravity	1.013	1.015
Total solids	3.02%	3.49%
Chlorids	3.00%	5.00%
Phosphates	3.50%	5.00%
Mineral sulphates	0.20%	0.40%
Urea	1.90%	1.30%
Ammonia	0.082%	0.035%
Uric acid	0.017%	0.020%
Creatinin	0.110%	0.068%
Albumin	0	0
Sugar	0	0
Indican	0	Trace
Diacetic	0	0
Acetone	0	0
Sediment	Neg.	Neg.

December 15: Since the attack of August 16 there had been a few minor attacks. On this date, however, there was loss of all movements of the right foot for several hours.

Table 2 is a comparison of the blood chemistry during this attack with that of a subsequent normal period.

TABLE 2.—*Blood Chemistry During Attack and During Normal Period*

(Mg. per 100 c.c.)	Dec. 15	Dec. 21
Urea	26	24
Uric acid	4.4	4.0
Creatinin	1.30	1.25
Total nonprotein nitrogen	29	25
Sugar	0.140	0.1125

DISCUSSION

Are we justified in calling this condition a mild form of family periodic paralysis? The usual textbook description of that disease leaves the impression that all patients have more severe attacks. Osler and McCrae,[1] for example, say:

> The clinical picture is similar in all recorded cases. The paralysis involves, as a rule, the arms and legs, but may be general below the neck. It comes on in healthy persons without apparent cause, and often during sleep. At first there may be weakness of the limbs, a feeling of weariness and sleepiness, but rarely with sensory symptoms. The paralysis, beginning in the legs, to which it may be confined, is usually complete within the first twenty-four hours. The neck muscles are sometimes involved and occasionally those of the tongue and pharynx. The cerebral nerves and the special senses are, as a rule, unaffected. The temperature is normal or subnormal, and the pulse slow. The deep reflexes are diminished, sometimes abolished, and the skin reflexes may be enfeebled. The faradic excitability of both muscles and nerves is reduced or abolished. Improvement begins within a few hours or a day or two, the paralysis disappearing completely and the patient becoming perfectly well. The attacks usually recur at intervals of one to two weeks, but they may return daily. They generally cease after the fiftieth year. There may be signs of acute dilatation of the heart during the attack.

Holtzapple,[2] who in 1905 reported seventeen cases in four generations of one family observed by him for twenty-two years, evidently found cases similar to ours. He says:

> The paralysis may be partial or complete, localized or general, the upper extremities alone or only the lower may be involved. It may be confined to the neck, or one half of the body may be completely paralyzed while partial paralysis affects the other half. The paralysis may be partial in the morning and become complete during the day. Some individuals may experience the heavy, sleepy, tired feeling, and sometimes a slight weakness in the extremities with an inco-ordination of the finer movements for days and in rare instances even a week, without the development of an attack. These are doubtless abortive attacks.

In view of this we feel justified in our diagnosis.

We can offer no new explanation as to pathogenesis. Since the first undoubted case was described in 1874 by Hartwig[3] there has been considerable work done, and several theories have been put forward.

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1. Osler and McCrae: The Principles and Practice of Medicine, Ed. 9. p. 931.

2. Holtzapple, G. E.: Periodic Paralysis, J. A. M. A. **45**:1224 (Oct. 21) 1905.

3. Hartwig: Ueber einen Fall intermittierenden Paralysis spinalis, Inaug. Diss., Halle, 1874 ref. by Bernhardt, Centralbl. f. d. med. Wissench. **13**:248, 1875.

Westphal,[4] Goldflam,[5] Oppenheim,[6] Crafts[7] and Singer[8] have found various abnormal appearances in excised muscle tissue. With the exception of Holtzapple, who favored "a vasomotor neurosis affecting the blood supply to the anterior horns," and Gatti,[9] who placed the disease in the group of hereditary myopathies, most investigators are inclined to believe in some toxic influence on the muscles, probably the result of disturbed metabolism. Edsall and Means[10] found evidence of this in 1915 and reviewed the previous work. Orzechowski[11] produced attacks in patients afflicted with this disease by injections of epinephrin. Schmidt[12] suggested that excessive epinephrin secretion, leading to transient ischemia in the muscles with accumulation of toxic material, produced the phenomena. Taylor,[13] Oddo and Audibert,[14] Cheinisse,[15] Kramer[16] and Gatti have collected the published cases. The last case found is that of Neustaedter,[17] who discusses the theories in full. He says: "The place of the lesion is indisputably in the muscles, but its character and modus operandi are still not demonstrated."

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4. Westphal: Ueber einen Fall von periodischer, auftretenden Lähmung, Berl. klin. Wchnschr. **22**:489, 1885.

5. Goldflam: Ueber eine eigentümliche Form von periodischer, familiärer wahrscheinlich autintoxicatorischer Lähmung, Wien. med. Presse **31**:1418, 1890; Ztschr. f. klin. med. **19**:240, 1891; Deutsch. Ztschr. f. Nervenheilk. **7**:1, 1895; **11**:242, 1897.

6. Oppenheim: Neue Mitteilungen ueber den von Prof. Westphal beschriebenden Fall von periodischen Lähmung aller vier Extremitäten, Charité Ann., **16**:350, 1891.

7. Crafts and Irvin: A Fifth Case of Family Periodic Paralysis, Am. J. Med. Sc. **119**:651, 1900.

8. Singer and Goodbody: A Case of Family Periodic Paralysis, Brain, **24**:257, 1901.

9. Gatti: La Paralysie Periodique, Gaz. d. hôp., Paris **84**:1327, 1911.

10. Edsall and Means: A Case of Family Periodic Paralysis, Am. J. Med. Sc. **150**:169, 1915.

11. Orzechowski, Ref. Neurol. Centralbl. **29**:622, 1910.

12. Schmidt, A. K. E.: Die paroxysmale Lähmung, Monographie 18; Aus dem Gesamtgebiete der Neurologie und Psychiatrie, Berlin, 1919.

13. Taylor, E. W.: Family Periodic Paralysis, J. Nerv. & Ment. Dis. **25**: 637, 1898.

14. Oddo and Audibert: La Paralysie periodique familiale, Presse méd., Paris **1**:256, 1902.

15. Cheinisse: La paralysie periodique familiale, Semaine méd., Paris **24**: 113, 1904.

16. Kramer, V. V.: Zur Frage der periodischen Paralyse der Extremitäten, Russ. med. Rundschau **6**:454, 1908.

17. Neustaedter, M.: A Case of Family Periodic Paralysis, Trans. of the Sect. on Nerv. & Ment. Dis. of the A. M. A., 1921.

Our case is submitted in order to place on record another instance of this rare disease and also to call further attention to its existence in a mild form.

NOTE.—Since presentation of this paper, in view of the finding of Orzechowski, the theory of Schmidt and the slight hyperglycemia shown in our case, the patient was given hypodermic injections of 1 and 1.5 c.c. of epinephrin, respectively, on two successive days. While he noted the usual sympathetic effects on blood pressure, pulse, pupils, etc., and felt some fatigue, numbness and deep soreness in the leg muscles, no paralysis resulted.

MORPHOLOGIC CHANGES IN NERVE CELLS FOLLOWING INJURY TO THEIR AXONS*

F. M. NICHOLSON, PH.D.

CHICAGO

Changes in nerve cell cytoplasm with its correlated axon and dendritic processes, together with changes in the size, shape, position and general character of its various constituents—the Nissl bodies, canalicular apparatus, mitochondria and the nucleus with its contained chromatin material and nucleolus—have been investigated repeatedly in connection with a number of variously induced methods of injury. For the most part, the changes described have been swelling, shrinkage, vacuolation and pigmentation of the cytoplasm; chromatolysis of the Nissl substance; fragmentation and dispersion of the canalicular apparatus; stability of the mitochondria; swelling, shrinkage, distortion, eccentricity, nuclear wall degeneration, vacuolation and increase or decrease in chromatin content of the nucleus; and increase or decrease in the number or size of the paranucleoli and nucleoli. The methods of inducing injury have been, in general, either direct, such as sectioning, tearing or stimulating electrically the axon processes, or indirect, as in inflammations, infections, chemical poisonings, various diseases of the nervous system, experimental anemia, fatigue, etc. Almost all of the changes enumerated above have been associated heretofore with practically every one of the various modes of injury outlined, but they have been so variable within such wide limits that it has been impossible to know with any degree of certainty just what the changes are for a given condition at a given time, and in many instances the findings have been contradictory.

In this connection it is interesting to find, from a brief review of the literature, that swelling and subsequent shrinkage of nerve cells were first described by Onuf [1] as being associated with the acute stage of cellular reaction to cutting of the axon processes, that such swelling was ascribed to be the first change to take place in cells under the two dissimilar influences of toxemia [2] and following sectioning of their

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* From The Hull Laboratory of Anatomy, The University of Chicago.

1. Onuf, B.: The Biological and Morphological Constitution of Ganglionic Cells, as Influenced by Section of the Spinal Nerve Roots or Spinal Nerves, J. Nerv. & Ment. Dis. **22**:597, 1895.

2. Berkley, H. J.: Studies on the Lesions Produced by the Action of Certain Poisons on the Nerve-Cell, Med. News, New York **67**:225, 1895.

axons,[3] and that Ballet and Dutil [4] obtained similar shrinkage in lumbar cord cells after compressing the abdominal aorta for five minutes. In electrical stimulation of nerves, Hodge [5] observed from 24 to 51 per cent. shrinkage, and Mann [6] found cytoplasmic swelling in sensory cells as early as thirty minutes after stimulation of the ganglion by electric means.

Vacuolation of the cytoplasm of lumbar nerve cells was observed by De Buck and De Moor [7] six hours after compression of the abdominal aorta for one hour, and by Marinesco [8] seventeen hours after a similar procedure, while after strychnin poisoning Holmes [9] found vacuolation within five and one half hours.

Cytoplasmic pigmentation, likewise, has been associated with various kinds of injuries to nerve cells.

Following cutting of axons, chromatolysis was described by Warrington [10] as early as ten days later—which became more advanced after fourteen days. Barker [11] found marked central chromatolysis after the fifteenth day, and MacCurdy [12] claimed that the changes were greatest between the twentieth and thirty-eighth days. Marinesco's [8] finding chromatolysis four days after tearing the axons is what one would expect on account of the more severe injury. However, chromatolysis within thirty minutes after electrical stimulation to ganglion cells by Mann [6] and seventeen hours after ligation of the abdominal aorta by Marinesco [8] is rather astonishing, yet Ballet and Dutil [4] claimed that changes in the Nissl substance are the first to take place in nerve cells in their reaction to axon injury.

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3. Williamson, R. T.: The General Pathological Histology of Nerve Cells, Med. Chron. Manchester, Ser. 4 **6**:17, 1903-1904.

4. Ballet, G., and Dutil, A.: Sur quelques lésions expérimentales de la cellule nerveuse, Comp. rend. cong. internat. de méd., Moscow, Sect. 7 **4**:260, 1897.

5. Hodge, C. F.: Some Effects of Electrically Stimulating Ganglion Cells, Am. J. Psychol. **2**:376, 1888-1889.

6. Mann, G.: Histological Changes Induced in Sympathetic, Motor, and Sensory Nerve Cells by Functional Activity, J. Anat. & Physiol. **29**:100, 1895.

7. De Buck, D., and De Moor, L.: Lésions des cellules nerveuses sous l'influence de l'anémie aigue, Le nérvraxe, Louvain **2**:1, 1901.

8. Marinesco, G.: Recherches sur la structure de la partie fibrillaire des cellules nerveuses a l'état normal et pathologique, Rev. neurol. **12**:405, 1904.

9. Holmes, G.: On Morphological Changes in Exhausted Ganglion Cells, Ztschr. f. allegem. Physiol. **2**:502, 1902-1903.

10. Warrington, W. B.: On the Structural Alterations Observed in Nerve Cells, J. Physiol. **23**:112, 1898-1899.

11. Barker, L. F.: On Certain Changes in the Cells of the Ventral Horns and the Nucleus Dorsalis (Clarkii) in Epidemic Cerebro-Spinal Meningitis, Brit. M. J. **2**:1839, 1897.

12. MacCurdy, H.: Degeneration in the Ganglion Cells of Cambarus bartonii Gir, Science **27**:916 (June 12) 1908.

Redispersion of the canalicular apparatus began by the seventh and reached its highest degree on the sixteenth day following sectioning of nerves, as has recently been accounted by Penfield.[13]

That the mitochondria in nerve cells are resistant to injury and retain their normal form and abundance has been shown especially by Clark,[14] Strongman [15] and McCann.[16]

As regards alterations in the nuclei, Mann [6] found these to become enlarged thirty minutes after electrical stimulation to ganglion cells.

It is also interesting to find that shrinkage of the nucleus was noted by Flemming [17] after cutting nerves, by Hayem [18] after tearing the axons, and that Hodge [19] found from 22 to 75 (with an average of 40) per cent. shrinkage of the nucleus after electrical stimulation of nerves from one to twelve hours, respectively, and that the degree of shrinkage varied directly with the time of stimulation.

Marinesco [8] also noted that ovaling of the nucleus took place at each stage of two and one-half, four, ten and twenty-nine days following tearing of the axon processes of motor cells.

After cutting of axons Marinesco [20] observed eccentricity of the nucleus within seven days, while a like phenomenon after fourteen days was described by Warrington.[10] Marinesco [21] found nuclear eccentricity of lumbar cord cells four and one-half hours after ligation of the aorta, and three and five days, respectively, after injection into the spinal ganglion of 2 per cent. sodium chlorid solution and 40 per cent. serum.

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13. Penfield, W. G.: Alterations of the Golgi Apparatus in Nerve Cells, Brain **43**:290, 1920.

14. Clark, E.: Regeneration of Medullated Nerves in the Absence of Embryonic Nerve Fibers Following Experimental Non-Traumatic Degeneration, J. Comp. Neurol. **24**:61, 1914.

15. Strongman, B. T.: A Preliminary Experimental Study on the Relation Between Mitochondria and Discharge of Nervous Activity, Anat. Rec. **12**:167, 1917.

16. McCann, G. F.: A Study of Mitochondria in Experimental Poliomyelitis, J. Exper. Med. **27**:31, 1918.

17. Flemming, R. A.: Some Notes on Ascending Degeneration (So-Called) and on the Changes in Nerve Cells Consequent Thereon, Brit. M. J. **2**:918, 1896.

18. Hayem, G.: Des altérations de la moelle consécutives a l'arrachement du nerf sciatique chez le lapin, Arch. de Physiol. Norm et Pathol. **5**:504, 1873.

19. Hodge, C. F.: A Microscopic Study of Changes Due to Functional Activity in Nerve Cells, J. Morphol. **7**:95, 1892.

20. Marinesco, G.: Des polynévrites en rapport avec les lésions secondaires et les lésions primitives des cellules nerveuses, Rev. neurol. **4**:129, 1896.

21. Marinesco, G.: Lésions des cellules nerveuses produites par les variation expérimentales de la pression osmotique, Ztschr. f. allg. Physiol., Jena **8**:121, 1908. Also Footnote 8.

Fragmentation of the nuclear membrane took place in nerve cells, according to Warrington,[10] fourteen days after cutting of the peripheral nerves.

Both reduction and increase in amount of nuclear chromatin following the use of various depressants were reported by Dolley,[22] but these were also dependent on duration and degree of action maintained.

Although most investigators mention no change from the normal, paranucleoli were observed to have increased in number following the experimental procedures employed by Marinesco,[23] Pariani[24] and Scarpini.[25]

In contradistinction to Flemming's[17] claim that the first evidence of axon reaction to appear in the nerve cell is a decrease in the size of the nucleolus, Mann[6] found this structure to become swollen in sensory cells thirty minutes after electrical stimulation of the ganglion. And, since Hodge[5] had observed that nucleoli decreased in number from motor cells following electrical stimulation, it is noteworthy that Warrington[10] found this structure frequently to break up and disappear as several smaller fragments within fourteen days after division of the axons.

It is thus seen that there are great variations in results observed by investigators employing various modes of injury, and that the nerve cells react in a totally different manner, depending on the kind, degree and time of action of the injury applied.

Although the changes named above have been investigated following a variety of experimental procedures, no complete study has ever been made following ligation of the axons. Furthermore, no one has ever made a study of a complete series of changes at regular intervals of twenty-four hours after a constant degree of injury and over a period of time sufficiently long to insure a knowledge of the final outcome of the injured cells. The necessity for such an investigation, the results of which may be used as a basis for future studies and interpretations of different degrees of axon reaction, is, therefore, plainly evident. It was with this purpose in view that the following investigation was undertaken, and in addition, to answer these questions: (1) What is

22. Dolley, D. H.: The Morphology of Functional Depression in Nerve Cells and Its Significance for the Normal and Abnormal Physiology of the Cell, J. Med. Res. **29**:65, 1913-1914.

23. Marinesco, G.: Recherches sur le noyau et le nucléole de la cellule nerveuse a l'état normal et pathologique, J. Psychol. u. Neurol., Leipzig **5**:151, 1905.

24. Pariani, C.: Ricerche interno alla struttura fibrillare e in seguito a lesioni dei nervi, Riv. di patol. nerv. e. ment., Firenze **10**:315, 1905.

25. Scarpini, V.: Sulle alterazioni delle cellule nervose nell'impertermia sperimentale studiate con i metode di Donaggio, Riv. sper. di freniat., Reggio-Emelia **32**:725, 1906.

the behavior of the various cytoplasmic constituents after injury to the axons of motor cells? (2) How soon after injury to the axon does the cell show changes in the various constituents? (3) At what stage of the reaction are the maximum changes manifest? (4) Just when and in what manner does the cell begin to regenerate? (5) What is the range of variability during the degeneration and regeneration stages? (6) How long does it take for the cell to recover completely from the injury? (7) What are the differences in the various cellular reactions to axon injuries of a mild nature, such as ligation of the axon, as compared with the changes in more severe injuries, such as tearing of the nerve, which is sure to kill the nerve cells?

MATERIAL AND METHODS

Common white rats, *Mus norvegicus-albinus,* weighing approximately 175 gm. each were employed. These were kept under the usual normal conditions before and after the operation, which was performed aseptically. The hypoglossal nerve and its nucleus cells were chosen for observation of the axon reaction because of their easy accessibility and bilateral unities. The axon reaction was studied under the two experimental procedures of ligation and of tearing the axons. In the former method the nerve in each animal was ligated at a point midway between its foramen of exit from the skull and the attachment of the posterior belly of the digastric muscle to the hyoid bone, caution being exercised not to produce traction on the nerve. In the latter method the nerve was torn apart in its deeper moorings after having been freed from the surrounding connective tissue, similarly as above. When the designated time had elapsed, the medulla containing the hypoglossal nuclei was carefully removed as quickly as possible and fixed in 95 per cent. alcohol for forty-eight hours. After dehydration the specimens were cleared in cedarwood oil and embedded in paraffin. Serial sections 6 microns thick were stained by the hematoxylin method of Macallum.[26] In each specimen the cells of the normal unit were studied side by side in the same section with those of the injured unit.

OBSERVATIONS AND DISCUSSIONS

The uninjured cells from the hypoglossal nucleus, properly fixed and stained, may be studied as representatives of typical motor nerve cells. These cells are stellate in outline and embody the contained cytoplasm in which are present the Nissl granules, axon hillock, dendritic processes and the nucleus with its nucleolus and oxychromatin bodies—each in normal relation to the other. The cytoplasm fills the whole of the cell space, including the axon and dendritic processes, and

26. Macallum, A. B.: A New Method of Distinguishing Between Organic and Inorganic Compounds of Iron, J. Physiol. **22**:92, 1897-1898.

shows no shrinkage areas or vacuoles after usual dehydration (Fig. 1). The irregularly shaped, but sharply defined basichromatin granules of Nissl occur in various sizes and are scattered uniformly throughout the cytoplasm except in the axon hillock, which is relatively large, and from which the rest of the cell substance is sharply defined. In the mid-zone of the cytoplasm these granules are slightly larger and more numerous than elsewhere (Fig. 1). They are separated from the nucleus and the cell wall by a narrow zone in which the granules are smaller and fewer. In the dendritic processes the Nissl bodies are filamentous, smaller, fewer than in the cell body and run parallel with the long axis of the process (Fig. 1).

The nucleus is a relatively large round body centrally located and ordinarily presents no indentations into nor protrusions from its surface (Fig. 1). It contains no substance, except the nucleolus, which is stainable by the Nissl method. However, an iron containing oxychromatin material is present in the form of a large irregular mass gathered nearest the axon side, numerous small round granules evenly distributed in the nucleoplasm, or both, which are demonstrable by the Macallum [26] hematoxylin method, according to Scott [27] and Nicholson [28] (Fig. 1).

The nucleolus, likewise a round and sharply defined body which may be centrally located, but which is frequently seen slightly nearer the axon side of the nucleus, stains intensely by the Nissl method (Fig. 1). If cut through its center, this body naturally appears larger than when cut tangentially, as may be demonstrated by serial sections. Its position probably has no significance—tending to settle with reference to gravity —as shown by Dahlgren.[29]

MORPHOLOGIC CHANGES IN THE NERVE CELLS FOLLOWING LIGATION OF THE AXONS

Changes in the nerve cells following ligation of their axons were studied at intervals of from one day up to sixty days and thereafter at intervals of from one month up to six months. In this complete series it was observed that the changes progress gradually from within the first day of reaction up to the fifteenth day (Figs. 2 to 16) after which regeneration begins and progresses gradually from the sixteenth up to the forty-four day after ligation, when the cells again become normal

27. Scott, F. H.: On the Structure, Micro-Chemistry and Development of Nerve Cells, with Special Reference to their Nuclein Compounds, Trans. Canad. Inst. **6**:405, 1899.

28. Nicholson, F. M.: Changes in Amount and Distribution of the Iron-Containing Proteins in Nerve Cells Following Injury to their Axones, J. Comp. Neurol. **36**:37, 1923.

29. Dahlgren, Ulric: Structure and Polarity of the Electric Motor Nerve-Cell in Torpedoes, Publication No. 212, Carnegie Institution, 213, 1915.

(Figs. 17 to 43). These two general phases may again be divided into substages as follows: (1) first to third days, (2) fourth to eighth days, (3) ninth to fifteenth days, and (4) sixteenth to forty-fourth days—for each of which a detailed account is given below. Similar stages were also designated, as regards most changes, by Dolley.[30]

The Cytoplasm.—In the cytoplasm, changes are apparent within twenty-four hours after axon ligation, when one of the first noticeable changes accompanying the axon reaction is the swelling of the cytoplasm, which is evident by the increase in size and ballooning of the cells observed in fresh or frozen sections and by the shrinkage observed in fixed preparations. The shrinkage areas are thus seen as small or large spaces, as illustrated in Figures 2 to 43 and 55 to 61. Occasionally shrinkage is seen all around the cell (Fig. 24) while in others it is shown only in certain small or large areas (Figs. 31 and 34). It is at first slight (Fig. 2) but increases in degree gradually up to the ninth day (Fig. 10), the beginning of the third stage. Usually it is present at places between the cell processes and seldom about them. Probably this is because the processes offer resistance to the cytoplasm on account of their connective tissue attachments.

From the ninth to the forty-fourth day of injury the degree of shrinkage remains marked (Figs. 10, 13, 16, 20 to 22, 24, 27 to 31, 34, 39 and 41), but presents considerable individual variations, however, because not all cells are affected alike. Some show greater shrinkage than others, which may be explained in part by the differences in plane of sectioning.

The shrinkage is present in some instances between the forty-fourth and fiftieth days, but it is little in amount and more nearly like that which is occasionally present in the first few days of the reaction.

That this swelling is due to an increase in fluid, most likely water, is shown by the fact that after dehydration of the preparations, the cytoplasm exhibits shrinkage away from the walls of the cell space, thus leaving clear spaces of various sizes and shapes between the axon and dendrites. It is possible that the increase in water content in the cytoplasm is imbibed from without, but it is more likely the result of oxidation of the cytoplasmic materials—probably the fats and sugars—during increased activity. In the fixed preparation this water is removed in the process of dehydration preparatory to mounting, thus leaving the shrinkage spaces. This is also in accordance with Lugaro,[31] Legendre [32]

30. Dolley, D. H.: The Neurocytological Reaction in Muscular Exertion, Am. J. Physiol. **25**:151, 1909-1910. Also Footnote 22.

31. Lugaro, E.: Sur les modifications des cellules nerveuses dans les divers états fonctionnels, Résumé, Arch. ital. de biol., Turin **24**:258, 1895-1896.

32. Legendre, R.: Les lésions des cellules nerveuses, Bull. de l'Inst. gén. Psychol., Paris **10**:317, 1910.

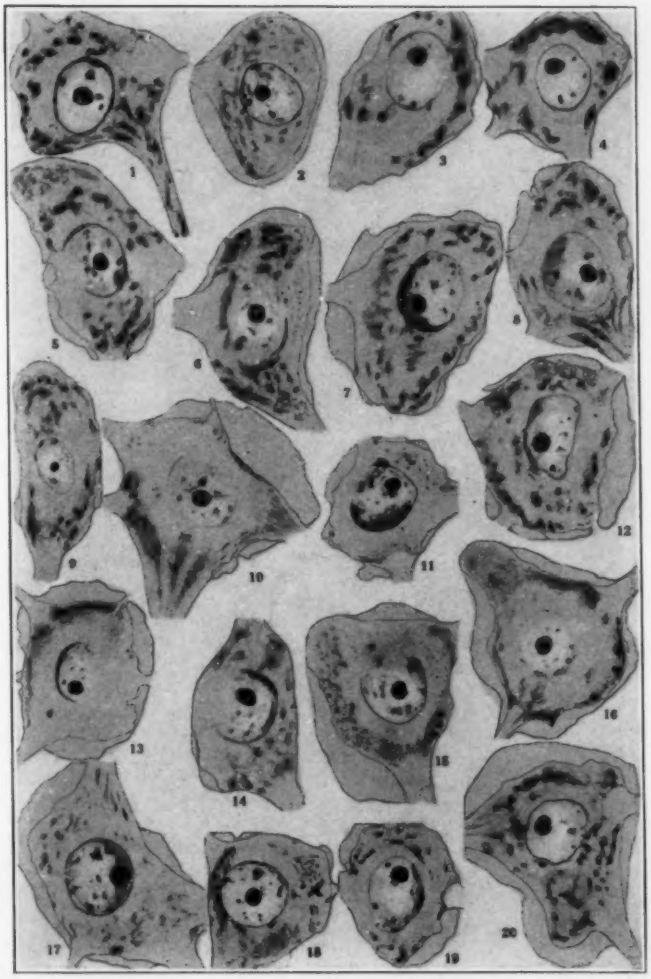

Fig. 1, normal hypoglossal nucleus nerve cell; Fig. 2, hypoglossal nucleus nerve cell after axon ligation duration of one day; Fig. 3, after ligation duration of two days; Fig. 4, of three days; Fig. 5, of four days; Fig. 6, of five days; Fig. 7, of six days; Fig. 8, of seven days; Fig. 9, of eight days; Fig. 10, of nine days; Fig. 11, of ten days; Fig. 12, of eleven days; Fig. 13, of twelve days; Fig. 14, of thirteen days; Fig. 15, of fourteen days; Fig. 16, of fifteen days; Fig. 17, of sixteen days; Fig. 18, of seventeen days; Fig. 19, of eighteen days; Fig. 20, of nineteen days.

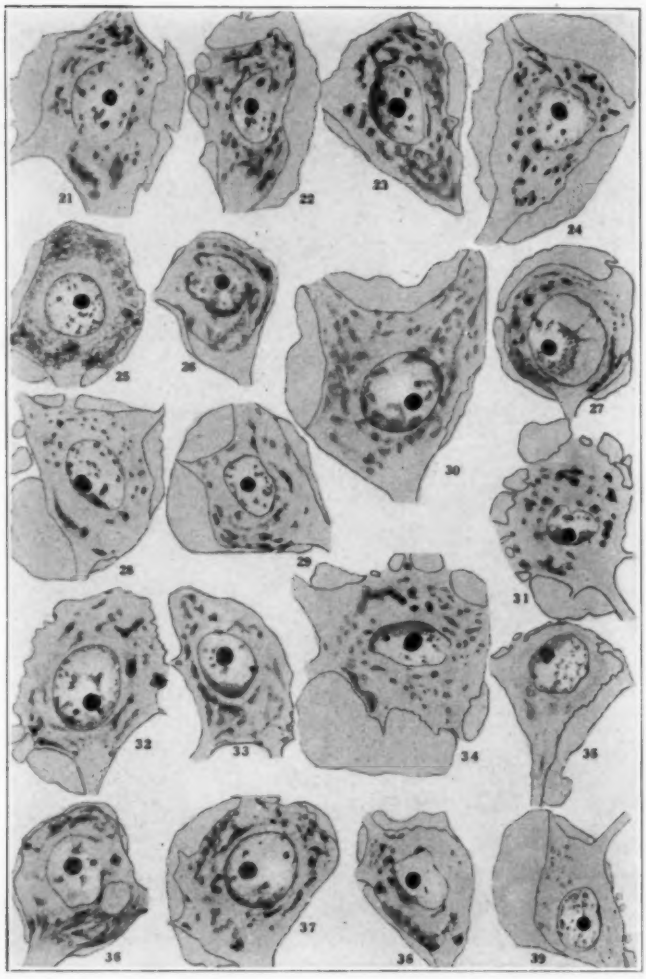

Fig. 21, after ligation duration of twenty days: Fig. 22, of twenty-one days; Fig. 23, of twenty-two days; Fig. 24, of twenty-three days; Fig. 25, of twenty-four days; Fig. 26, of twenty-five days; Fig. 27, of twenty-six days; Fig. 28, of twenty-seven days; Fig. 29, of twenty-eight days; Fig. 30, of twenty-nine days; Fig. 31, of thirty-one days; Fig. 32, of thirty-two days; Fig. 33, of thirty-three days; Fig. 34, of thirty-four days; Fig. 35, of thirty-six days; Fig. 36, of thirty-seven days; Fig. 37, of thirty-eight days; Fig. 38, of thirty-nine days; Fig. 39, of forty days.

and Dolley,[33] who each held the view that the cells became swollen owing to increased activity.

Vacuolation and pigmentation of the cytoplasm were not observed in this investigation. Regarding the former, it may be conjectured that much that has been called "vacuolation" may have been artefact change or nothing other than what we term shrinkage areas of one size or other in the periphery of the cytoplasm. Concerning the pigmentation, undoubtedly this may occur in old injuries of a severe nature.

Within twenty-four hours after axon ligation, the Nissl bodies begin to disappear from the cytoplasm immediately around the nucleus by first becoming smaller on the side nearest the axon and then gradually dispersing peripherally (Fig. 2), as was also described by Flemming.[17] In the second and third days of reaction there is a definite clear zone about the nucleus and the Nissl bodies become enlarged first, like those described by Goldscheider and Flatau,[34] and then enmass in the periphery of the cell (Figs. 3 and 4). This is a picture typical of beginning "central chromatolysis" and corresponds with that described first by Onuf [1] and later by Faure.[35]

From the fourth to the eighth days of reaction there is a subsidence of the chromatolysis and the large peripheral masses again break up into smaller granules which exhibit an appearance of fragmentation (Figs. 5 to 9). This stage was noted also by Onuf [1] and Marinesco.[8] While this process is going on it is also evident that the Nissl material increases in amount about the axon hillock, as seen especially in Figures 6 and 7, and likewise described by Dolley.[22] This period following the first frantic efforts of the axons to regenerate, as shown by Cajal,[36] also corresponds with certain stages described by Dolley.[37]

The stage in which the most marked changes occur is that between the ninth and fifteenth days, as represented in Figures 10 to 16, and observed previously by Warrington.[10] In this stage the Nissl material disappears rapidly and progressively from the whole of the cytoplasm except close to the cell wall where it accumulates in heterogeneous masses along with a few scattered smaller granules (Figs. 10, 11, 13 and 16). Barker [11] found the same degree of degeneration at the fifteenth day after sectioning nerves. In cells represented by Figures 11

33. Dolley, D. H.: Further Verification of Functional Size Changes in Nerve Cell Bodies by the Use of the Polar Planimeter, Anat. Rec. **11**:349, 1916-1917.

34. Goldscheider, A., and Flatau, E.: Weitere Beiträge zur Pathologie der Nervenzellen, Fortschr. d. Med., Berlin **16**:211, 1898.

35. Faure, M.: L'acellule nerveuse et le neurone; structure et functions a l'état normal et pathologique, Gaz. d. hôp., Paris **72**:781, 1899.

36. Cajal, S. Ramón y: Studien über nervenregeneration, 1, 1908.

37. Dolley: Footnotes 22 and 30.

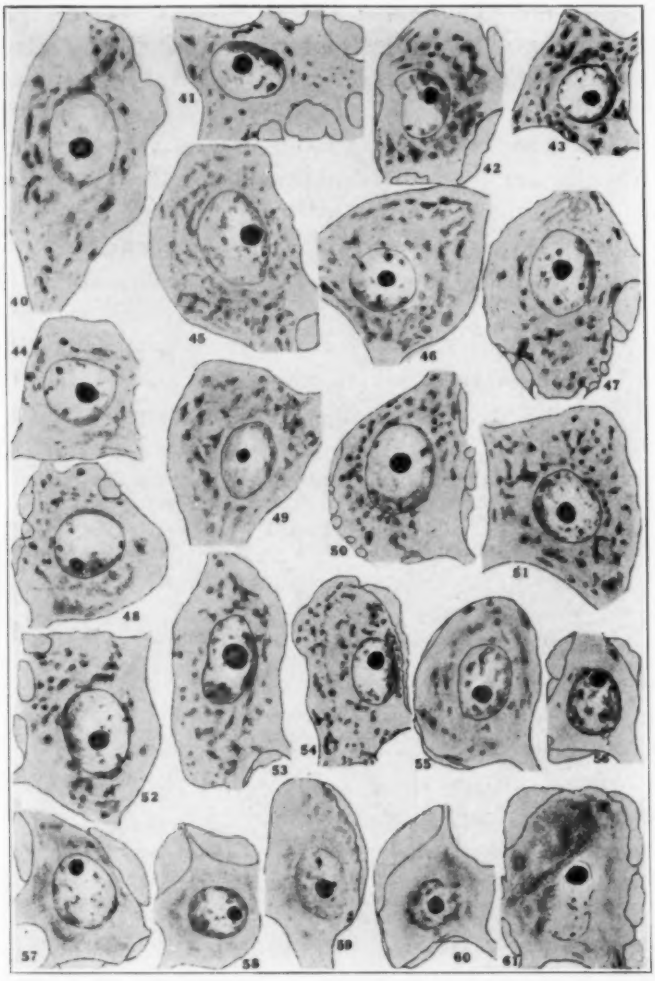

Fig. 40, after ligation duration of forty-one days; Fig. 41, of forty-two days; Fig. 42, of forty-three days; Fig. 43, of forty-four days; Fig. 44, of forty-five days; Fig. 45, of forty-six days; Fig. 46, of forty-seven days; Fig. 47, of forty-eight days; Fig. 48, of forty-nine days; Fig. 49, of fifty days; Fig. 50, of two months; Fig. 51, of three months; Fig. 52, of four months; Fig. 53, of five months; Fig. 54, of six months; Fig. 55, five days after tearing the axons; Fig. 56, ten days after tearing the axons; Fig. 57, fifteen days after tearing the axons; Fig. 58, twenty days after tearing the axons; Fig. 59, twenty-five days after tearing the axons; Fig. 60, thirty days after tearing the axons; Fig. 61, thirty-five days after tearing the axons.

and 13 almost the whole of the cytoplasm is free from Nissl substance, while in all those represented in this stage the substance has accumulated about the axon hillock to a greater extent than in the preceding stages—particularly so in Figures 10 to 13 and 15 to 16, as had been observed by McCarthy.[38] This is the stage of advanced "central chromatolysis" and is precisely like the several stages described by Dolley.[37] At the same time the axon hillock becomes progressively smaller. Whether this is real or due merely to shrinkage of the cytoplasm, especially that about the axon hillock, is a question.

Beginning at the sixteenth day and continuing to the forty-fourth day of axon reaction to ligation, regenerative changes take place. The Nissl granules again reappear in the cytoplasm, first near the nucleus (Fig. 17), as described by Flemming[17] and Faure,[35] and then increase in number and size gradually until the cell is, to all appearances, again normal (Fig. 43). At first these granules are small (Figs. 17 to 19), but gradually they become larger and fill the mid-zone of the cytoplasm, as shown in Figures 1 and 43. While this material continues to remain increased in amount around the axon hillock in the earlier days of regeneration (Figs. 18, 19, 25 and 27), it gradually assumes the normal amount in the later days (Figs. 28 to 43). This again agrees substantially with the changes described in the various stages by Dolley.[37] The Nissl substance remains normal from the forty-fourth day to six months after axon ligation.

The depletion and repletion of Nissl substance is commensurate with the views held by the physiologists, namely, that the chromatin represents a storehouse for nutritive material which is depleted during activity of the cell and is replaced on rest, although this view is wholly inadequate, since it does not consider all the factors involved in cellular activity regarding which so little is known.

For obvious reasons the changes in canalicular apparatus and mitochondria were not investigated in this series.

The Nucleus.—In the first stage of nuclear reaction to axon ligation it is evident by the second day that the nuclear wall undergoes change by loss of its stainable substance in two places (Fig. 1), as described first by Flatau[39] and Marinesco.[20] Within the nucleus there is a reduction in size and number of granules of oxychromatin material and a

38. McCarthy, D. J.: Peculiar Types of Ganglion Cell Degeneration, Univ. Pa. Med. Bull. **20**:15, 1907-1908.

39. Flatau, E.: Einige Betrachtungen über die Neuronenlehre im Anschluss and frühzeitige, experimentell erzeugte Veränderungen der Zellen des Oculomotoriuskerns, Friedländer, Fortschr. d. Medicin **14**:201, 1896.

distribution of these close to the nuclear membrane (Figs. 3 and 4) similar to that observed by Mott,[40] Pugnat [41] and Dolley.[42]

From the fourth to the eighth days, namely, during the second stage, the nuclear chromatin granules are again increased to beyond the normal in amount, size and distribution (Figs. 3 to 9), also described by Marinesco [23] and Dolley,[43] except in the nuclear wall where it continues to remain deficient at a point farthest from the axon (Figs. 5 and 6). Sometimes the nuclear chromatin increase is marked by a large mass of material collected on the axon side (Fig. 7). This increase was also observed first by Flatau.[39] In this stage the nucleus exhibits distortion of its surface (Figs. 7 and 8) like that described by Barker,[11] Marinesco,[44] Whitwell [45] and Pugnat.[41]

In the third stage of axon reaction, from the ninth to the fifteenth day, the nuclear chromatin again becomes decreased as characterized especially by the small granules exhibited in Figures 10, 12, 13 and 16 (first noted by Dolley [22] and Mott [40]) and the loss of stainable substance from the nuclear wall gradually becomes more and more marked up to the fifteenth day when it disappears entirely and corresponds in degree with the cytoplasmic changes (Figs. 4 to 16). Warrington [10] described a similar change at the fourteenth day after sectioning of nerves. In these cells there is no appreciable increase in chromatin material on the axon side of the nucleus except in Figure 11. Accompanying these changes is a gradually corresponding irregularity of the nuclear outline (Fig. 7).

As soon as the degenerative changes reach the maximum in degree at the fifteenth day, the nuclei begin to regenerate. The whole stage of regeneration lasts from the sixteenth to the forty-fourth day, at which time the nuclei become normal in every respect (Figs. 17 to 43). The oxychromatin material gradually becomes increased, as characterized by the reappearance of granules of various shapes and sizes uniformly

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40. Mott, F.: The Psychopathology of Puberty and Adolescence, J. Ment. Sc. **67**:279, 1921.

41. Pugnat, M.: Des modifications histologiques des cellules nerveuses dans l'tat de fatigue, Compt. rend. cong. internat. de méd. e. ment., Paris, sect. d'histologie **52,** 1900.

42. Dolley, D. H.: The Morphological Changes in Nerve Cells Resulting from Over-Work in Relation with Experimental Anemia and Shock, J. Med. Res. **21**:95, 1909.

43. Dolley, D. H.: The Recovery from Depression in the Purkinje Cell and the Decline to Senility of Depression, with the Incidental Histogenesis of Abnormal Pigmentation, J. Comp. Neurol. **28**:465, 1917. Also Footnote 22.

44. Marinesco, G.: Sur la chromatolyse de la cellule nerveuse, Interméd. d. Biol., Paris **1**:514, 1897-1898.

45. Whitewell, J. R.: Nuclear Vacuolation in Nerve Cells of Cortex Cerebri, Brain **12**:520, 1889-1890.

scattered throughout the nucleoplasm (Figs. 17 to 43). In Figure 28 the small rounded granules are most conspicuous, while in Figure 30 large irregular ones predominate. In Figure 27 it appears that the granules may possibly be formed from the nucleolus and are then dispersed peripherally. The large mass of nuclear chromatin usually seen in the axon side of the nucleus of cells again becomes characteristic in those undergoing regeneration. This is seen especially in Figures 17, 19, 23, 26, 28, 30 to 35, 37, 41, 42 and 43. Although the nuclear wall on the side farthest from the axon is still unstainable in the earlier days of regeneration (Figs. 19, 21, 22, 24 and 26), it certainly becomes normal toward the forty-fourth day following (Fig. 43). On the other hand, the nucleus remains somewhat distorted throughout the whole period of regeneration (Figs. 19, 20, 22, 24, 26, 31, 34, 36, 38 and 42), but becomes normal thereafter.

From the forty-fourth day to the sixth month after axon injury the nucleus continues to remain normal in every respect (Figs. 43 to 54).

Such phenomenon as swelling and shrinkage of the nucleus may be explained on the same basis as similar changes in the cytoplasm.

Distortion of the nucleus is most likely due secondarily to the shrinkage of this structure.

Although eccentricity of the nucleus was not significant in our preparation, it may well be added that such phenomenon, when present, is probably also a secondary one, due to fluidity changes in the cytoplasm following severe injuries, since Stuurman [46] found eccentricity only after marked cytoplasmic changes. Most investigators found that the nucleus became markedly eccentric—even to the point of bulging from the cell body, and in some cases, to extrusion. But the type of injury employed by them was more severe than usual, such as cutting, which was done by Onuf,[1] Ballet and Dutil [4] and Marinesco,[44] or as tearing the peripheral nerve as was done by Hayem [18] and Marinesco,[5] strong electrical stimulation, poisonous drugs and infectious diseases.

Fragmentation of the nuclear wall and increase or decrease in chromatin content of the nucleus, likewise, are best accounted for according to the conception of the physiologists regarding chromatin as storage material necessary to cellular activity, although entirely inadequate.

The Nucleolus.—No change from the normal was observed in the size, shape or position of the nucleolus, although Lugaro [31] found this structure increased in size during increased activity of the cell and decreased during fatigue.

The Axon.—The axon hillock becomes smaller, progressively, from the eighth up to the fifteenth day of axon reaction (Figs. 9 to 16),

46. Stuurman, F. J.: Zur Kenntniss der tigrolytischen Ganglienzellschwellung, Neurol. Centralbl. **34**:856, 1915.

after which it again becomes normal in size gradually, from the sixteenth to the forty-fourth days (Figs. 17 to 43), being smallest in the stages of greatest axon reaction (Figs. 17 to 21). The most marked change in size of the hillock is, therefore, between the eighth and twentieth days (Figs. 9 to 21). Associated with this decrease in size is an accumulation of Nissl substance in the cytoplasm immediately around the hillock (Figs. 9 to 21). But since there is a shrinkage of the cytoplasm in this stage, it is questionable whether this decrease in size of the hillock is real or due merely to shrinkage, especially that about the hillock (Figs. 2 to 39). After the forty-fourth day of reaction and up to six months the axon remains normal in size and character.

The Dendrites.—No pathologic changes were observed in the dendrites in any stage of the axon reaction to ligation.

MORPHOLOGIC CHANGES IN THE NERVE CELL FOLLOWING TEARING OF THE AXON

Nerve cells react quite differently to varying degrees of axon injury. To mild injuries the cells exhibit but slight degenerative changes, while to severe injuries the degeneration becomes extremely marked—to the extent that the cells themselves degenerate completely and die. It was shown in the foregoing account that, although the degenerative changes were rather marked, the injury was not severe enough to produce death to the cells, but that they instead returned to normal. It was therefore considered desirable to study the reaction changes following injury sufficient to produce complete degeneration and to compare them with the ligation experiments. In order to do so the axons of the hypoglossal nerve cells were torn apart close to the foramen of their exit from the skull after the nerve had been carefully exposed and freed from its moorings. Striking differences were observed in these cells as compared with those in which ligation was performed. These changes were studied at intervals of five days up to fifty days of axon reaction, when it was discovered that all the cells became completely degenerated by the thirty-fifth day.

The Cytoplasm.—Shrinkage of the cytoplasm is slight five days after tearing, but becomes more marked after ten days, and reaches its highest degree by the fifteenth day and remains so until death of the cell at the thirty-fifth day. (Compare Figs. 55 to 61 with Figs. 2 to 43.)

The Nissl granules diminish from the cytoplasm gradually from the first up to the twentieth days, when they disappear entirely (Figs. 55 to 58). Five days after tearing of the axons the Nissl granules are fewer in number and smaller in size than in the normal cell (Fig. 55), although their distribution is quite like that in the normal cell and the degree of reaction is slightly less at this stage in this type of injury than five days after axon ligation. Compare Fig. 55 with Fig. 6.) This is

probably due to the absence of the great and usually transient regeneration activity in the first four or five days after injury as described by Cajal.[36] By the tenth day, the tearing reaction practically equals that of the ligation reaction at the tenth day. (Compare Fig. 56 with Fig. 11.)

Fifteen days after tearing, the Nissl substance is almost completely gone (Fig. 57), and twenty, twenty-five, thirty and thirty-five days after axon tearing the Nissl material is entirely depleted (Figs. 58 to 61, respectively). Many of these changes correspond with the axon tearing experiments of Marinesco.[8] After this period the cells are dead and beyond recognition, except for a few whose axons were not included in the tearing procedure. At no stage in this form of reaction is there an accumulation of Nissl substance in the periphery of the cytoplasm nor about the axon hillock similar to that observed in the ligation experiments (Figs. 55 to 61).

The Nucleus.—Following axon tearing, the changes in the nuclear chromatin are at first less marked than after ligation, because after five, ten and fifteen days the chromatin remains normal in amount, size of granules and distribution (Figs. 55 to 57). But after the twentieth day the changes are more marked—characterized at first by an increase in amount in the periphery of the nucleoplasm (Fig. 58), which is followed at the twenty-fifth day by a marked decrease with only a few small granules remaining (Fig. 59). By the thirtieth and thirty-fifth days of reaction even these disappear, and the cells are dead (Figs. 60 and 61). The nuclear membrane likewise disappears, the nucleus as a whole becomes distorted in outline (Figs. 60 and 61), and after this stage no part of the cell is longer recognizable.

The Nucleolus.—No change from the normal nor that of the ligation procedure was observed in the size, shape or position of the nucleolus (Figs. 55 to 61).

The Axon.—No change was noted in the axon hillock, which becomes unrecognizable as soon as the Nissl material becomes depleted, even as early as the fifth day of the reaction.

The Dendrites.—Along with the cytoplasmic degeneration there is a parallel change in the substance on the dendrites, Nissl bodies disappearing entirely.

SUMMARY AND CONCLUSIONS

1. From the foregoing observations it is evident that changes in the structural elements of motor nerve cells following injury to their axons take place in a rather definite manner, and that these are different under the two dissimilar modes of injury—namely, that of ligating and that of tearing the axons. The differences in reaction changes under these two experimental procedures are due, solely, to the difference in the degree of injury employed.

2. The reaction of nerve cells to axon injury of a mild nature, such as ligation, is characterized by two general phases of degeneration and regeneration. The former begins within twenty-four hours and progresses gradually up to the fifteenth day after injury, whereas the latter begins at the sixteenth day and progresses gradually up to the forty-fourth day after maintained injury, when the cells again become normal in every respect. It is thus seen that the reparative stage is twice as long as that of degeneration. In both of these all of the nerve cell constituents are involved, with the exception of the nucleolus. One of the first of these degenerative changes is the swelling with subsequent shrinkage of the cytoplasm, which begins within twenty-four hours and gradually increases in degree and reaches its maximum by the ninth day after injury. This degree of shrinkage is then maintained throughout the whole of the rest of the phases of degeneration and regeneration until the forty-fourth day, when the cells become normal. Coexistent with the onset of swelling is the "central chromatolysis" which begins immediately around the nucleus, especially on the side nearest the axon, while large masses of Nissl substance form in the periphery of the cytoplasm. From the fourth to the eighth day these large masses fragment and scatter, while in the meantime there is a further reduction in the amount of Nissl material progressively from the nucleus toward the periphery. During this period cytoplasmic chromatin accumulates around the axon hillock, which diminishes in size. During the period from the ninth to the fifteenth day practically all of the cytoplasm becomes free from Nissl bodies except for occasional small and scattered granules, and a further accumulation of chromatin about the axon hillock which continues to diminish in size. As the reparative changes take place from the sixteenth to the forty-fourth day, small granules of Nissl substance at first appear in irregular and scattered form close to the nuclear membrane, from whence they become increased gradually and progressively from the center toward the periphery of the cell. These granules become more numerous, larger in size and more regular in shape and distribution, and most abundant in the mid-zone of the cytoplasm until the forty-fourth day, when their appearance is in every respect like that of the normal cell. Thus the Nissl substance is both depleted and replaced, first, in the vicinity of the nucleus, thence spreading peripherally. No changes were noted in the Nissl bodies in the dendrites.

3. The nuclear reaction to axon ligation exhibits a decrease in chromatin material during the first three days, after which it increases to an amount beyond the normal until the eighth day, particularly on the side nearest the axon. This is again followed by a decrease to below the normal amount from the ninth to the fifteenth day, at which time it is most marked and coincides with the marked decrease in Nissl

substance from the cytoplasm at the same stage. From the sixteenth to the forty-fourth day there are slight increments in some cells, but in most of them the return to normal in amount and distribution is gradual up to the forty-fourth day. In most of the later stages it again becomes increased on the axon side of the nucleus. Other phenomena in the nuclear reaction exhibited at the same time are inability of staining reaction of the nuclear wall and distortion of the whole nucleus, both of which are most marked from the ninth to the fifteenth days.

4. It is thus seen that the degenerative changes in all the cellular constituents studied begin within twenty-four hours and reach the maximum between the ninth and fifteenth days of axon reaction and that the regenerative changes begin at the sixteenth day and continue to the forty-fourth day, when the cell recovers completely from the injury.

5. Under the condition of tearing of the axons the degenerative changes are slightly more accentuated and the stages are longer. Marked shrinkage of the cytoplasm is present throughout, and the Nissl bodies gradually become depleted uniformly throughout the cytoplasm, including the dendrites, from the first up to the twentieth days, when they completely disappear. In so doing the axon hillock gradually becomes unrecognizable. The nucleus shows an increase in chromatin up to the tenth day and a decrease only after the fifteenth day of reaction and continues gradually up to the thirty-fifth day, when all the chromatin has disappeared and such cells are undoubtedly dead. At the same time the nucleus becomes distorted and the nuclear wall is completely fragmented. In this condition, then, the nucleus undergoes degeneration later than the cytoplasm, while during the ligation procedure the two are coincident.

All figures were drawn with the aid of Zeiss apochromatic objective 1.5 mm., compensating ocular No. 12 and camera lucida at table level. Since they were reduced two-thirds they represent a magnification of 700 diameters. All of the preparations were fixed in 95 per cent. alcohol diluted from specially prepared absolute alcohol, and the blue-black microchemical color reaction was obtained by the Macallum hematoxylin method.

INVOLUNTARY MOVEMENTS: THEIR UNUSUAL ASSOCIATION AND RELATION TO THE PHENOMENA OF DECEREBRATE RIGIDITY *

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Neurologists have been making fairly definite classifications of cases into well-known clinical syndromes, but analysis of the host of dyskinetic disorders which accompanied the acute forms of epidemic encephalitis or remained as chronic sequelae has shown such unusual combinations and fragmentation of the involuntary movements as to render classification almost impossible. We would draw attention to (1) the various combinations of abnormal involuntary movements in the same patient; (2) manifestations of fragments of dyskinetic syndromes in others; (3) the differences of the same type of involuntary movements in different patients and in the same patient at different times; (4) the presence of phenomena hitherto unassociated with the more or less well defined syndromes, and (5) the occurrence in definitely organic disease of movements which, because of their pattern-like character, have hitherto been regarded as psychogenic in nature.

In view of Walshe's recent dogmatic limitation of the phenomena of decerebrate rigidity to lesions of the pyramidal pathways,[1] (a statement to which we take decided exception), it is necessary to discuss the relationship of those phenomena to involuntary movements and the extrapyramidal syndromes.

The two following cases illustrate the coexistence of numerous types of involuntary movements in the same individual.

REPORT OF CASES

CASE 1.—*An instance of so-called double athetosis presenting choreiform, athetoid and dystonic movements, together with postural disturbance (a fragment of decerebrate rigidity).*

I. C., a girl, aged 8½ years, complained chiefly of the presence of abnormal movements and inability to walk or to sit up. Birth, at full term, was difficult and instrumental. She had pneumonia at 2, pertussis at 3 and measles at 5. Her illness apparently began at 6 months of age with generalized purposeless movements, which have gradually become more marked up to the present. At the ages of 2 and 5 and at irregular intervals since, the child has had generalized convulsions.

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* Read before the New York Neurological Society, Dec. 4, 1923.

1. Walshe, F. M. R.: The Decerebrate Rigidity of Sherrington in Man, Arch. Neurol. & Psychiat. **10**:1 (July) 1923.

Physical Examination.—She is unable to sit or hold up her head. There are irregular, purposeless choreiform movements of all muscles of the body and slightly of those of the face; occasional athetoid movements occur in the fingers and toes. There is a distinct dystonic element in all the movements, which are greatly exaggerated by purposeful activity and emotional states. Associated movements are observed in the upper extremities on attempting to move the lower, and vice versa; one also notes occasional associated facial movements. The upper extremities are frequently extended, and the hands turned outward; so, too, the lower extremities are extended and the feet plantar-flexed. Her speech is an unintelligible, monotonous drawling jargon.

All other neurologic, general, physical and laboratory data are negative.

CASE 2.—*A combination of choreiform, parkinsonian and tic-like movements following epidemic encephalitis, engrafted on which is a hysterical astasia-abasia.*

R. E., a girl, aged 18, who gave a history of an acute attack of epidemic encephalitis in September, 1920, followed by a period of emotional distress, showed on examination one year later, bilateral ptosis, nystagmus, slight weakness of the right face, and the following hyperkinetic phenomena: (1) rhythmic movements of the forearms (supinator-pronator action) parkinsonian in type; (2) choreiform twitchings of both index fingers and thumbs; (3) a jerky adductor movement of both shoulders, associated with internal rotation of the arms; (4) a lateral tic-like jerk of the head; (5) astasiabasia.

In this connection reference may be made to the occurrence of parkinsonian tremor in a typical case of dystonia musculorum deformans.[2]

The next two cases illustrate the second point, namely the manifestation of fragments of certain dyskinetic syndromes.

CASE 3.—*An instance of a choreodystonic type of movement confined to the musculature of the right foot. (Three years have elapsed with no progress of the disorder.)*

G. W., a Russian Jewess, aged 28, married four and a half years, whose past history, except for influenza and pneumonia in 1918, is irrelevant, and in whose family there is no history of a similar illness, became suddenly ill three years ago (1920), without apparent cause. Peculiar involuntary movements of the right foot and toes appeared, which interfered with walking. There are no other complaints.

Examination.—The general physical examination gives negative results. The points worthy of note in the neurologic examination are: (1) Peculiar, twitch-like, choreiform involuntary movements involving all the toes of the right foot. These toes "fan" and go into plantar flexion, in a frequently repeated movement. This interferes with walking to the extent of causing a slight limp. There is also a very slight tendency to the assumption of the equinovarus position. (2) The paradoxical phenomenon of J. Ramsay Hunt. (3) More active right knee-jerk than left; equally active Achilles tendon reflexes; no Babinski sign. (4) No definite weakness or atrophy. (5) Negative serology.

There is nothing about this patient to suggest a functional element. The movements are always the same and are unrelated to any emotional factor either in onset or course.

CASE 4.—*A remarkable dyskinetic syndrome following epidemic encephalitis, belonging to the dystonia group, segmental in nature and limited to the head and*

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2. Wechsler, I. S., and Brock, S.: Dystonia Musculorum Deformans, Arch. Neurol. & Psychiat. **8**:538 (Nov.) 1922.

neck musculature. The retracted head, opisthotonic back, pronated hand and equinus foot, form an exquisite example of decerebrate rigidity. In fact, the clinical picture is one of recurring waves of partial decerebration.[3]

S. D., an American boy of Italian parentage, aged 11, who had pneumonia at 2, and in whose family there is no history of any chronic illness, became ill April 28, 1922, with headache, fever and abdominal pain. On the following day the left eye was "turned in" and the boy "saw double." He became drowsy, the fever continued and his entire body "shook" so that he was unable to stand. At St. Vincent's Hospital, New York, the diagnosis of acute epidemic encephalitis was made. One month later the mother noted salivation and some difficulty in swallowing. Then seizures appeared in which his neck became hyperextended, his mouth opened and the eyeballs turned upward. There was no accompanying loss of consciousness. These attacks have persisted since and are of variable occurrence and duration. The boy has never had vesical disturbance.

Examination, June, 1923.—In the recumbent position the boy's head is turned to the left and flexed slightly on the right shoulder. The right upper extremity is flexed at all joints, the palm of the hand faces outward, and the thumb is drawn backward and outward. There is adduction and inward rotation of the right arm, with almost complete pronation of the right hand. The left hand also shows this extension of the terminal phalanges of the thumb. The trunk is opisthotonic (*C* in the accompanying illustration); there is contraction of the hamstrings; the abdomen shows spasm of the recti muscles, and the right toe is in constant dorsal extension.

When sitting, the boy shows a very decided plantar flexion and inward rotation of the left foot and toes (talipes equinovarus position) and to a lesser extent of the right. There is a spasmodic tendency of the head to be drawn backward with the chin rotated to the left, involving the sternomastoid and the posterior neck muscles.

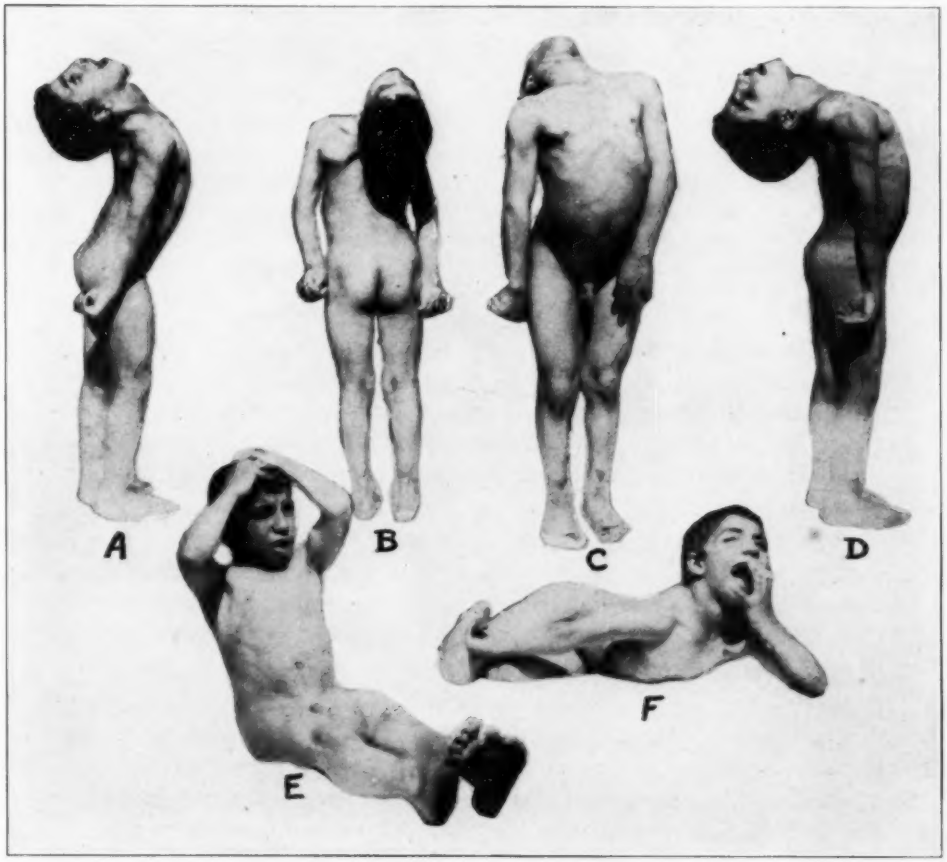
Seizures.—The attack is as follows: first, there is an upward rotation of the eyes, then the lids half close, the forehead overwrinkles, the mouth gapes open, the upper lip is drawn upward, the lower jaw is drawn downward by the spasm of the depressor muscles of the mandible, the head is rotated backward until the occiput almost touches the interscapular region (*A* and *B* in the accompanying illustration). The right hand becomes everted, the right arm rotated inwardly (*A, B, C* and *D*). Conjoint rotation of eyes to the right and fibrillary twitchings of the tongue are noted. This position is interrupted by the patient drawing his head forward voluntarily with the aid of his hands (*E*). In fact, he brings his head forward repeatedly after it has been thrust back, and with his fingers he pulls down his upper lip and closes his gaping mouth by pushing the mandible up (*F*). This movement is requently repeated. The face is drawn up in a spasmodic movement, not as frequently as the lips, head and other parts. While these "larger" head movements, lasting five or ten seconds, are repeated at irregular intervals, there are other interrupted smaller excursions consisting merely of a partial thrusting back of the head and partial opening of the mouth. With this, too, the patient voluntarily brings forward the retracted head and closes the gaping mouth.

While the boy seems to overact these clownish movements, they are repeated in a stereotyped pattern. Numerous observations disclose the same movement even when the boy does not know that he is being watched. For instance, while

3. This patient was presented at the meeting of the Section of Neurology and Psychiatry of The New York Academy of Medicine, Oct. 9, 1923.

playing ball in the garden of the hospital with other children, the same twisting distortion was noted. On the other hand, there are times when the movements are quite minimal, which is in striking contrast to the days when the movements are marked.

His gait is quite unaffected. He can jump and run up and down stairs with considerable agility. Between seizures his upper extremities swing normally in walking; during them the upper extremities, especially the right, lose their associated swing.



Postures and movements during the seizures in Case 4.

Cranial Nerves: The left pupil is greater than the right; both are irregular and react very sluggishly to light and in accommodation. The fundi and fields of vision are normal. The left palpebral aperture is greater than the right. There is a very fine rapid lateral nystagmus, marked vertical nystagmus on upward gaze and less on downward gaze. Convergence is very poorly done. While the motor and sensory trigeminals are normal, the lateral movements of the lower jaw are poorly performed. The jaw jerks are very lively. Hearing is normal, and labyrinthine tests give normal reactions. The palatal movements are poorly performed, but there is a good palatal reflex. The tongue deviates

to the left and shows fine fibrillations and coarse tremors, especially on the right. There is marked hypertrophy of the sternomastoids, especially on the right. Resistance of the posterior neck muscles to passive movement and increased muscular development of the shoulder girdles and neck are noted. Between seizures there is a slight hypertonus to passive movements on the right. During an attack this hypertonus increases.

Reflexes: The deep reflexes of the upper extremity are all equal and lively. The abdominals and cremasterics are very lively. The knee and Achilles tendon jerks are lively and equal; there is no ankle clonus. There is a bilateral Babinski sign, the right greater than the left. The finger-to-nose test is well performed with eyes open and closed. There is apparent adiadokokinesis on both sides, probably due to slowness rather than clumsiness of movement. A rapid, fine tremor of the extended upper extremity is noted. At times respiration is deep and labored; occasionally the accessory muscles are involved. The speech is somewhat nasal and monotonous. Sensory examination is negative, as are all serologic and laboratory findings. No Magnus and DeKleijn neck reflexes can be elicited *between seizures.* Dr. I. Abrahamson interprets the attack itself as a kind of *spontaneous Magnus and De Kleijn neck reflex, the dorsal movement of the head setting up decerebrate postures in the extremities.*

Case 4 presents signs of diffuse multiple lesions of the brain stem from the basal ganglia down to the lower medulla. The occurrence of upward conjugate movements of the eyes, with closure of the lids in the beginning of the seizure, points to the hypothalmic region. Of particular interest is the fact that we are dealing with a segmental dystonia, which has developed as a sequel to an undoubted attack of epidemic encephalitis.

We have previously commented on the association of decerebrate rigidity phenomena with the syndrome of dystonia musculorum deformans[2] In Case 4 this association is exquisitely demonstrated; in fact, the dyskinetic element in the case is really due to waves of decerebrate posture which sweep over him. Strangely enough, however, the gaping mouth, with its downwardly retracted jaw, is at variance with the picture of decerebrate posture, for in this latter condition the jaws are usually closed.

It should be pointed out that the occurrence of a dystonic movement does not stamp the case as one of dystonia musculorum deformans, as the case just presented illustrates. Here we are dealing with *"segmental (fragmentary) dystonia"* in contradistinction to the full-blown dystonia musculorum deformans. On the other hand, analysis of a typical case of dystonia frequently shows a tendency to segmental involvement, particularly in the early days of the disease.

With regard to phenomena not usually associated with dyskinetic syndromes, mention may be made of an atypical case of multiple sclerosis in which a definite dystonic movement is present. Again, in a girl, aged 8 years, with acute chorea involving the right side only, there was loss of associated movement of the right upper extremity in walking,

and eversion (pronation) of the right hand. No pyramidal tract signs and no weakness could be demonstrated.

It may be pointed out that the preceding cases illustrate the inadequacy of our terminology and the impossibility of fitting cases into established syndromes, such as the choreas, double athetosis, dystonia, etc. Without discussing for the present the accuracy of the descriptive terms themselves, it may be stated that they do not designate diseases or syndromes, but merely signs or symptoms. And just as headache and cough are not diseases, neither are chorea and athetosis. And when, as in the foregoing observations, numerous abnormal involuntary movements of different types are seen in the same individual, the terminology becomes confusing.

RELATION OF INVOLUNTARY MOVEMENTS TO PHENOMENA OF DECEREBRATE RIGIDITY

Since the appearance of S. A. K. Wilson's paper,[4] phenomena of decerebrate rigidity have been described in connection with various clinical pictures. Wilson called attention to the presence of so-called "fragments of decerebrate rigidity" in chorea and dystonia musculorum deformans. In a series of six cases of the latter affection, we supplemented Wilson's original observation. The validity of these findings has been seriously questioned by Walshe.[1] It is our opinion that some of his exceptions are not well taken and that his sweepingly dogmatic statements are not warranted by the facts at hand.

Briefly, decerebrate rigidity is a term applied by Sherrington to a peculiar tonus state of the musculature in mammals following cross-section of the midbrain between the anterior and posterior colliculi. It is characterized by a heightened tone of the extensor groups of muscles. As described by Sherrington,[5] such a decerebrate animal "hangs with its fore limbs thrust backward, with retraction at shoulder joints, straightened elbow and some flexion at wrist. The hand of the monkey is turned with its palmar face somewhat inward. The hind limbs are similarly straightened and thrust backward; the hip is extended, the knee very stiffly extended, and the ankle somewhat extended. The tail . . . is straight or often stiffly curved upward. There is little opisthotonus of the lumbosacral vertebral region. The head is kept lifted against gravity, and the chin is tilted upward under the retraction and backward rotation of the skull on the neck. The mouth is kept closed and there is some stiffness in the elevators of the jaw."

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4. Wilson, S. A. K.: On Decerebrate Rigidity in Man and the Occurrence of Tonic Fits, Brain **43**:220, 1920.

5. Sherrington, C. S.: The Integrative Action of the Nervous System, Yale University Press, 1906.

The rigidity of the "antigravity muscles," capable of maintaining the animal in the standing position, does not require the presence of the cerebellum or nucleus ruber.[6] That it depends on some structure in the pons or the upper medulla, *possibly the vestibular nuclei and the descending vestibulospinal tracts,* is shown by the important fact that section of the brain stem in the medulla below the level of the calamus scriptorius, destroys the extensor rigidity. In its stead there appears a flexor flaccidity incapable of maintaining the animal in the standing position. Walshe would limit the application of the extensor physiologic state in man to cases showing: (1) "spasticity of pyramidal tract lesions, . . . (with) a proprioceptive reflex reaction . . . showing reciprocal innervation"; (2) the plasticity with lengthening and shortening reactions; (3) the presence of the phasic spinal reflex, as flexion of lower extremity with its Babinski sign and clonus, and (4) the presence of the tonic neck and labyrinthine reflexes of Magnus and DeKleijn.

In the main, Walshe stresses the *quality* of the rigidity, the pattern being of lesser importance. To an extent this is justifiable. Such "tonic fits" as tetanus and strychin poisoning do not belong in the decerebrate rigidity category. As Sherrington has shown, these tonic rigidities are due to a riotous overthrow of reciprocal innervation at the lower level, i. e., the spinal arc.

In other words, given a rigidity due to extrapyramidal diseases with postural fixations resembling the pattern of decerebrate rigidity, as retracted head, pronated hand, opisthotonic back, and equinus foot, Walshe believes it should be thrown out of the decerebrate rigidity category because of the absence of *that essential quality "interference with the function of the pyramidal system."* The fact that we have a nonpyramidal rigidity with a tonus pattern identical with that of decerebrate rigidity, and that the brain level of the extrapyramidal disorder is close to the level of decerebrate rigidity, have no significance to Walshe. For him, "the extrapyramidal motor diseases . . . must be rejected as having no relation with decerebrate rigidity," because "of the absence of the essential interference with the function of the pyramidal system." It would seen to us that there are some pointed objections to this viewpoint.

It may be asked, if a lesion of the pyramidal tract alone is responsible for the phenomena of decerebrate rigidity, why must such a lesion be situated in the midbrain? The fact is that the pyramidal tract hemiplegia with its rigidity, reflex changes and Babinski sign is the

6. Bazett, H. C., and Penfield, W. G.: A Study of the Sherrington Decerebrate Animal in the Chronic as Well as the Acute Condition, Brain **45**:185 (1922).

same whether produced at the level of the colliculi, the medulla or upper cervical cord. And yet decerebrate rigidity follows section at the first level and not at the other two. Obviously, then, there must be a pathway or mechanism other than the pyramidal tract, which is not present below the upper level of the medulla, intereference with which results in the phenomena of decerebrate rigidity.

Very recently, Warner and Olmsted,[7] experimenting on cats, have shown the importance of a "cortico-ponto-cerebellar pathway" in connection with decerebrate rigidity. This tract has its origin in the frontal lobe, passes through the mesial part of the internal capsule, extends caudad past the level of the anterior corpora quadrigemina; the majority of the fibers then cross to the opposite side and enter the cerebellum by way of the middle cerebellar peduncle. Stimulation of this tract anywhere along its course inhibits decerebrate rigidity in a remarkably consistent way. It seems not unlikely that this rather than the pyramidal tract is the "essential tract," interference with which is so necessary for the production of extensor rigidity.

Walshe also states that no one "has recorded the occurrence of involuntary movements of the tremor, choreiform or athetosis varieties in the decerebrate animal." This is an obvious criticism of recent papers dealing with the presence of decerebrate rigidity phenomena in dyskinetic disorders. One must not forget that in the decerebrate animal we are studying the effects of a carefully planned surgical experiment which has as its sole purpose the production of one condition—decerebrate rigidity. It is quite obvious that in man this does not occur. Clinically, we meet conditions caused by inflammatory and heredodegenerative processes of long development and standing. Furthermore, the decerebrate rigidity phenomena are secondary, often fragmentary, and do not occupy the foreground of the picture.

In this connection, an interesting study is presented by I. L. Meyers.[8] He describes two human cases, in both of which detailed clinical and pathologic examinations were made. They showed both Magnus and DeKleijn and decerebrate rigidity phenomena, together with *involuntary movements*. Furthermore, it should be noted that in one of these cases clinical and pathologic investigation disclosed *no pyramidal tract disorder*, but lesions in the lenticular nuclei and cerebellum; the other showed lesions of the motor cortex and lenticular nuclei.

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7. Warner, W. P., and Olmsted, J. M. D.: The Influence of the Cerebrum and Cerebellum on Extensor Rigidity, Brain **46**:189 (July) 1923.

8. Meyers, I. L.: Magnus and DeKleijn Phenomena in Brain Lesions of Man: A Consideration of These and Other Forced Attitudes in the So-Called Decerebrate Man. Arch. Neurol. & Psychiat. **8**:383 (Oct.) 1922.

When such cases as the one we described (Case 4) show postural tonus-patterns similar to those present in the decerebrate animal, one can hardly believe that we are dealing with unrelated phenomena.

As to the presence of the Magnus and DeKleijn reflexes, further study of them is necessary in the dyskinetic syndromes. In the presence of involuntary movements, these tonic neck and labyrinthine reflexes are difficult of demonstration.

Admitting that the term decerebrate rigidity has been used loosely, we take distinct exception to Walshe's conception which insists that the condition be limited to lesions of the pyramidal tract. Our reasons have been given above. Granting that this extensor rigidity is a "release phenomenon," neither anatomicophysiologic nor pathologic facts indicate exactly the pathways involved; certainly nothing warrants the categorical assumption made by Walshe. Whatever the explanation, the fact remains that clinically one does observe phenomena showing *the pattern* of decerebrate rigidity in patients exhibiting abnormal involuntary movements and extrapyramidal syndromes. No one has conclusively shown that the *quality* of this extensor postural tonus pattern must be *the* specific hypertonus of pyramidal tract lesion.

Clinical and Occasional Notes

TUBERCULOUS MENINGITIS*

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C. A. PATTEN, M.D., Assistant Neuropathologist Philadelphia
General Hospital, PHILADELPHIA

The following case is reported because of several points of interest. In the first place, there is an association of an apparent psychoneurotic reaction with active tuberculous infection of the nervous system; secondly, the disease ran a rapid course, the symptoms being ameliorated by cistern dramage; and thirdly, a focus of possible origin was found in the middle ear and mastoid.

REPORT OF CASE

The patient, a white woman, aged 36 years, twice married, whose family history is unimportant, was admitted Feb. 27, 1922. The past history disclosed scarlet fever at the age of 10 accompanied by "brain fever" (delirium?) and followed by "running ears." Her first husband died of tuberculosis. The second marriage was contracted a few days prior to admission. Her family considered that she was neurotic and always exaggerated minor physical ailments. The present illness began Feb. 15, 1922, with intense headache. There followed diplopia, and mental symptoms; emotional uncontrol, apprehension and violence; later nausea and vomiting.

On admission the temperature was 98.4. The patient was agitated, emotional, apprehensive, complained of intense headache, pains in various parts of the body, and was overactive. Speech was clear, and relevant, the sensorium clear throughout. Memory, orientation, general information, and retention were without defect. She had no insight. Later she became delirious and disturbing. Spinal drainage relieved the headaches; this was performed first by the lumbar route, but later by cistern puncture. The spinal fluid showed a high pleocytosis: 610, 650, 496, and 440 cells per cubic millimeter on successive days. Neck rigidity and Kernig's sign had a tendency to disappear following drainage of from 20 to 30 c.c. of fluid, and on one occasion she immediately slept after puncture. Four days before death a cistern puncture failed to deliver fluid with the needle at the 5.5 cm. mark, but a few drops of blood appeared. A diagnosis of block above the cisterna magna suggested itself at this time. Death occurred March 20, 1922, following progressive failure and the development of bronchopneumonia.

The patient was obese with segmental distribution of fat. The chest examination revealed no evidences of tuberculosis. The fundi showed neuroretinitis and papilledema. There were bilateral sixth nerve paralysis, weakness of the lower right face, tongue deviation to the left, slow, hesitant speech, rigidity of the neck and bilateral Kernig sign.

Blood count showed a low red cell count, 9,200 leukocytes, 75 per cent. of which were polymorphonuclears. The Wassermann reaction was negative. There was a trace of albumin in the urine. The spinal fluid was under pressure; the cells were all lymphocytes; the colloidal gold curve was 0001221100; pellicle formation took place with negative smear and stain for tubercle bacilli. Guinea-

* From the Neuropsychiatric Department (Service of Dr. M. H. Bochroch), and Neuropathological Laboratory, Philadelphia General Hospital.

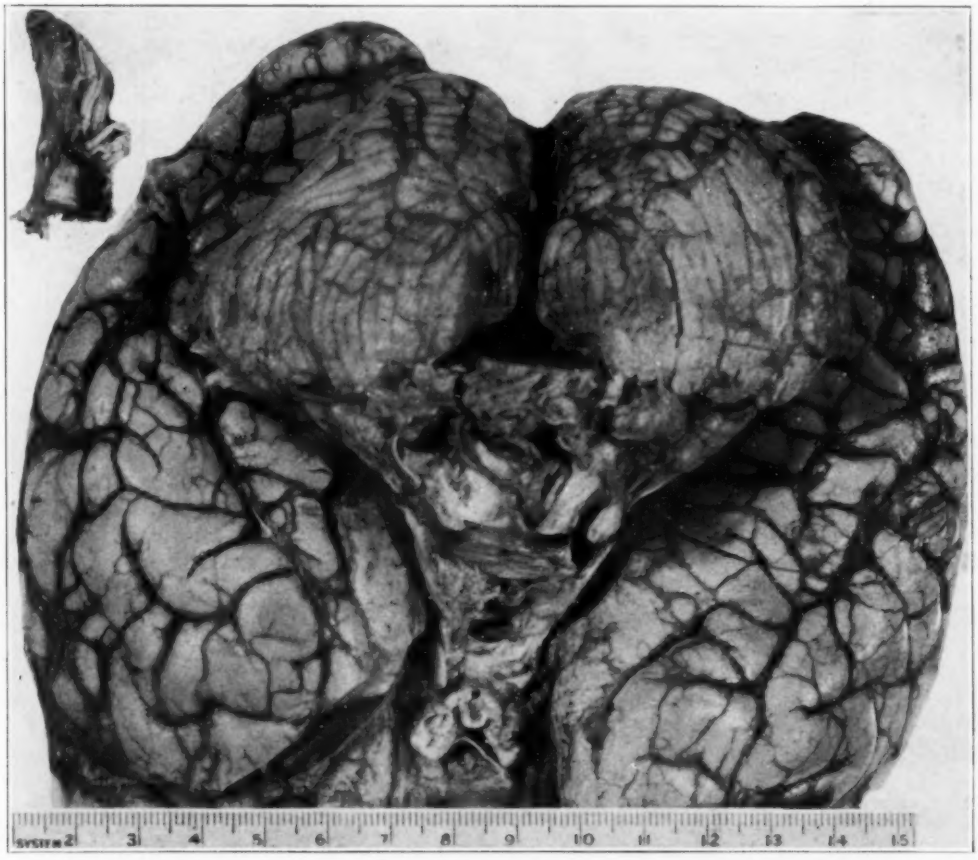
* Read before the Philadelphia Psychiatric Society, March 9, 1923.

pig inoculation was later reported negative. The temperature showed an evening rise, the highest point reached being 101.2 a week before death. The pulse ranged between 100 and 110; the blood pressure was 115 systolic, 110 diastolic.

The clinical diagnosis was tuberculous meningitis and bronchopneumonia, although epidemic encephalitis was also considered.

NECROPSY REPORT

Brain.—On removal of the calvarium and incision of the dura, the cortical surfaces of the brain were found to be absolutely dry. The venous channels



The figure at the left upper corner shows a small blood clot in the dorsal surface of the lower medulla. The large figure shows enormous pial thickening and exudative membrane over the pons, cerebellum and interpeduncular structures.

were distended with blood giving the pia a dark appearance. The dura was apparently normal. On removing the brain, the posterior fossa was found sealed off by a thick, yellowish exudative membrane. This evidently accounted for the dry cortical surfaces, as all channels of communication between the ventricular system and subarachnoid spaces of the cerebrum were cut off.

The posterior fossa contained a small amount of nonturbid cerebrospinal fluid. The interpeduncular space was covered by a thickened pia with a yellowish tough exudate, which veiled all the underlying structures and involved

many of the cranial nerves as shown in the accompanying illustration. This pial involvement extended somewhat over the temporal poles and backward over the pons and cerebellum, being particularly intense over the pons. In general the appearance of the pia suggested a chronic suppurative meningeal infection.

At the left posterolateral margin of the lower medulla a radical of the plexus of spinal veins was thrombosed, and the pia at this point punctured; a small blood clot, 1.0 x 0.5 cm., was adherent to the pia and to the dura at the margin of the foramen magnum of the same side (shown in the accompanying illustration). These findings are ascribed to the traumatism of the last unsuccessful cisterna magna puncture. Bilateral exposure of the middle ear and mastoid showed a necrotic process and a collection of a rather dry and thick pus in the right inferior mastoid cells and middle ear. No organisms were isolated from this. Microscopically, there was found a clear cut generalized tuberculous meningo-encephalitis with point of greatest intensity at the base. Careful search was made for predominance of polynuclear leukocytes but none was found, at least not more than would be expected in this type of infection. The most marked and frequent changes were found in the brain stem. The visceral necropsy revealed no tuberculous focus, or other pathologic change of note.

COMMENT

The question of an extension of tuberculosis from some focus contiguous to the brain structure must be considered in contradistinction to a vascular transmission of the disease from a focal point at some distance from the brain. Buzzard and Greenfield[1] state that tuberculous leptomeningitis is always secondary and never primary. Bing[2] holds the opinion that it is the most frequent variety of metastatic meningitis and always secondary to a lesion elsewhere. It less frequently arises by continuity, but tuberculous caries of the skull bones, tuberculosis of the ear, and solitary tubercle of the brain usually furnish a starting point. In this case the first impression that we were dealing with a secondary suppurative infection superimposed on a chronic tuberculous lesion of the meninges, gave place to the secondary consideration of a possible long standing tuberculous meningo-encephalitis secondary to a possible long standing chronic middle ear and mastoid tuberculosis. McCallum,[3] Crockett,[4] Bryant,[5] Goldstein,[6] and Oppenheimer,[7] have reported that this condition is occasionally seen. The history in the case shows that there had been an otitis media, more or less chronic, since the age of 10, which followed an attack of scarlet fever. The further statement that the patient had "brain fever" at this time cannot be considered significant in view of the possibilities of delirium concomitant with the exanthem and middle ear disease. The point then arises as to the possibility of a tuberculous infection of the middle ear and mastoid on the basis of a former chronic infection of another type. It is far more common, however, for a suppurative process to be superimposed on a chronic tuberculosis. A search for other foci of infection in the viscera proved unavailing. The primary focus then remains undetermined, providing we cannot accept the

1. Buzzard and Greenfield: Pathology of the Nervous System, Ed. 1, London, Constable and Co. Ltd., 1921, p. 167.
2. Bing: A Textbook of Nervous Dseases, New York, Rebman Company, 1915, p. 299.
3. McCallum: Textbook of Pathology, Ed. 1, Philadelphia, W. B. Saunders & Co., 1917.
4. Crockett, E. H.: Tuberculosis of the Middle Ear and Mastoid, J. A. M. A. **47**: 1293 (Oct. 20) 1906.
5. Bryant, W. S.: Tuberculosis of the Middle Ear and Mastoid, Med. Rec. **74**: 513 (Sept. 26) 1908.
6. Goldstein, M. A.: Primary Tuberculosis of the Ear, Med. News (March 14) 1903.
7. Oppenheimer: Pathology, Diagnosis and Treatment of Tuberculosis of the Middle Ear, Med. Rec. (June) 1900.

theory of its location in the middle ear. One argument in favor of the middle ear focus lies in the fact that the suppurative material found there was dry and cheesy, and contained no organisms. So far as could be determined, the process had not been active for a great many years.

Reports concerning spinal drainage in the treatment of brain infections are conflicting. For example, Kohte and Schlesinger [8] have obtained improvement in cases of tuberculous meningitis with spinal drainage. Deniges, Sabrazès and Wentworth [9] report that their cases were aggravated by this procedure.

However, we feel it was of benefit as a palliative measure in our case. It resulted on each occasion in a definite, transient relief from the severe headache. Cistern drainage was employed owing to the difficulty of lumbar puncture. The technic of cistern puncture as outlined by Ayer [10] was followed closely. The needle was inserted to an average depth of 5 cm., and when no fluid was found it was inserted cautiously to the 5.5 cm. mark where blood was obtained. Using the other eight punctures as controls the probability of a block above the cistern magna was considered. We did not consider, however, that an accident might have occurred. There was no marked change in the patient's general condition. A progressive increase in the papilledema was noted the week before death. An increase in intracranial pressure was definitely present judging by the increased papilledema following the cessation of cistern drainage. Of course this furnished a definite contraindication to cistern puncture, although we did not expect to find the extensive accumulation of fluid at the base of the brain with subsequent distortion and partial obliteration of the triangular space constituting the cisterna magna which was present. Cheney [11] reported a dry spinal subarachnoid space due to diffuse tuberculous infiltration of the spinal meninges. Sealing off of the posterior fossae obstructing free circulation of the cerebrospinal fluid is reported by Thompson.[12] Such an occurrence prevents relief of symptoms through spinal drainage.

SUMMARY

This report is of interest in that (1) the psychoneurotic elements present were found to be associated with an active tuberculosis of the central nervous system; (2) presumably a chronic otitis media and mastoiditis was the original focus of infection; (3) the transient beneficial effect of spinal and cisternal drainage is of therapeutic import. The puncture of a small vein in the region of the cisterna magna was of no consequence in the end result.

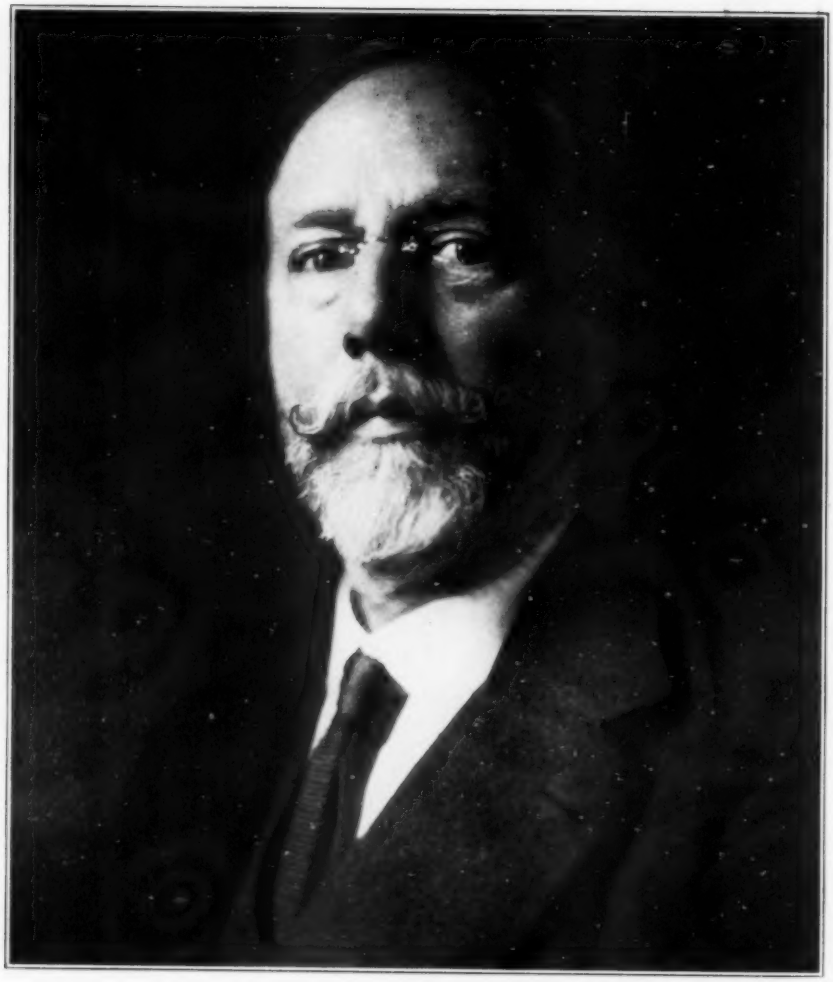
8. Kohte, and Schlesinger E.: Textbook of Nervous Diseases, translated by Alexander Bruce, Schechter & Co., 1911, Vol. 2, p. 786.

9. Deniges, Sabrazès, H., and Wentworth: Textbook of Nervous Diseases, 1911, Vol. 2, p. 786.

10. Ayer, J. B.: Puncture of the Cisterna Magna, Arch. Neurol. & Psychiat. **4**: 529 (Nov.) 1920.

11. Regan, J. C., and Cheney, G. W. H.: A Case of Tuberculosis Meningitis with a Dry Spinal Subarachnoid Space Due to Diffuse Tubercle Infiltration of the Spinal Meninges, Am. J. Dis. Child. **22**: 516 (Nov.) 1921.

12. Thompson, H. C.: Diseases of the Cerebral Meninges, Oxford Medicine, 1921, Vol. 6.



HENRY HUN

1854-1924

Obituary

HENRY HUN

1854-1924

Dr. Henry Hun, one of the most distinguished and honored members of our profession, passed quietly away at his home in Albany, N. Y., Friday evening, March 14, 1924, after an illness of only three days, a victim of lobar pneumonia. He would have been 70 years old the following Friday. Thus came abruptly to an end a professional career covering almost a half century and glowing to the last with the warmth of human kindness and the luster of scientific achievement. In his death, the city of Albany has lost one of its most illustrious and zealous citizens, and the medical profession one of its most learned and brilliant clinicians. Dr. Hun's life was one unbroken chain of effort and accomplishment, one unwearying vigil in the struggle of suffering humanity, one unending pilgrimage to the forge of science and progress. Endowed by nature with a wealth of talent and ability, possessed of a magnetic and commanding personality, gifted with unusual keenness of observation and judgment and eminently just and practical in his disposition of all problems, Dr. Hun was exceptionally well fitted for the prominent place which he held as a consultant, a teacher and an author.

Dr. Hun was born in Albany, March 21, 1854, the son of Dr. Thomas Hun, himself a most accomplished and eminent Albany physician who was on the first board of consulting physicians of the Albany Hospital when it was organized in 1848, and president of the New York State Medical Society in 1862. The Hun family is one of the oldest and most prominent families in Albany and traces its origin to Harmen Hun of Amersfoort, a town in the province of Utrecht, Holland, situated on the Eem river twenty-five miles southeast of Amsterdam. Harmen Hun had a son, Thomas, whose son, Harmen Thomas, came to America and then to Albany from Amersfoort and married Catalyntie Berck in 1661. In the succeeding generations down to Dr. Hun, his direct ancestors included members of the Van Rensselaer, Wendell, Gansevoort, Winne, Lansing, Bleecker, Schuyler and many other families of the early Dutch settlers.

Dr. Henry Hun received his first education at the Albany Academy, from which he graduated in 1870. He then attended the Sheffield Scientific School at Yale University, where he was awarded his degree of Ph. B. in 1874, after which he entered the Harvard Medical School,

receiving his degree of M.D., in 1879. His father then sent him abroad, where he spent two and a half years studying in various European capitals, perfecting his knowledge of medicine in general, but already evincing an irresistible leaning toward neurology, a field in which he was destined later to acquire fame and distinction. While in Paris, he became a pupil of Charcot and devoted most of his time to that great master's clinic and laboratory at the Salpêtrière.

After his return from Europe, Dr. Hun became connected with the Albany Medical College as well as with most of the hospitals of his native city, serving in the capacity of attending physician and neurologist. He plunged at once into the task of improving the standards of medical education, engaged in numerous clinical and pathologic researches and spent a considerable portion of his time studying and treating the chronic invalids in the humbler districts of Albany. This early manifestation of his unselfish nature won for him the enduring admiration and gratitude of the poorer classes, and although he soon commanded a most extensive and lucrative practice among the higher social strata, he always continued to exhibit toward the sick poor the same gallant spirit of concern and generosity. For this reason, Dr. Hun retained throughout his life the love and confidence of rich and poor alike, and his death brought desolation to the hearts of all. Very early in his career, Dr. Hun gained recognition and prestige by reason of his superior knowledge of medicine in general and of neurology in particular, and became a favorite and eagerly sought consultant throughout the central and eastern part of New York State. He was almost constantly grappling with the exigencies of a huge and trying practice. Not only did other physicians seek his opinion and advice in their baffling and obscure cases, but they likewise brought to him their own personal problems and miseries, so that he became known and highly esteemed as the physician's doctor, as one to whom the younger members of the profession could safely go with the full assurance of being cordially received and judiciously counseled.

As a teacher of medicine, Dr. Hun justly enjoyed a reputation which it is believed has rarely been equaled and perhaps never surpassed in this country. For a period of almost thirty years (1885 to 1914), he occupied the chair of neurology in the Albany Medical College, a post which he filled with extraordinary ability and almost religious zeal. By dint of untiring labor and unbounded enthusiasm, Dr. Hun succeeded in organizing a department of neurology, the efficiency and general excellence of which gained nation-wide recognition and attracted to the school many students from even remote parts of the country. Probably not far from a thousand physicians practicing in New York and in the various adjoining states received a most substantial part of their medical and neurologic training from him, and they gratefully

remember the teacher who strained every effort to develop their powers of clinical observation and to establish on a sound and practical basis the props of their professional future. And what an admirable and fascinating teacher Dr. Hun was! He seemed to embody all the attributes which serve to stamp the master. His distinguished appearance, his keen penetrating eyes, his clearly articulated and pointed phrases, his forceful method of presentation and his lucid and logical reasoning, all contributed to identify him as a man of towering strength whose presence tacitly imposed order and discipline and at the same time inspired respect and confidence. Moreover, a constant undercurrent of humor streaked with an irrepressible tinge of sarcasm rendered him both interesting and formidable. This characteristic trait, which was the delight of Dr. Hun's friends, was not infrequently the despair of the student unfortunate enough to wander unwisely into a maze of diagnostic blunder. The resulting discomfiture Dr. Hun invariably capitalized in his favorite scheme of driving home even more forcibly the cardinal importance of the objective finding under display or of the diagnostic point which he wished to emphasize. He was one of the first, if not the first, to conceive the idea of holding clinics and conferences at which the student himself presented a case previously assigned to him and postulated a diagnosis thereafter subject to criticism and correction by the teacher as well as to queries and discussion by the rest of the class. The practical advantages of such a method of teaching can hardly be overestimated and were fully appreciated by the eager and enthusiastic pupils who crowded Dr. Hun's lecture room and clinics.

As an author, Dr. Hun has indelibly written his name in the history of American medicine. To him we owe a unique volume entitled "An Atlas of the Differential Diagnosis of the Diseases of the Nervous System," a work of unusual merit and originality, which has proved of immense service to students and practitioners alike, as is well attested by the fact that it ran through three editions. He was also the author of a "Syllabus of a Course of Lectures on the Diseases of the Nervous System," a practical notebook in two volumes for students, which has been regularly used by them in the Albany Medical College since its first appearance in 1901. In addition, Dr. Hun contributed to literature a series of over thirty monographs on different topics of medical or neurologic interest, all of the highest order and some of them of the utmost scientific value. It would far exceed the scope of the present biography to attempt an adequate appraisal of this imposing array of scientific publications,[1] but in all fairness one cannot fail to mention

1. A complete list of Dr. Hun's contributions will appear in a history of the American Neurological Association soon to be published on the occasion of the Association's Fiftieth Anniversary.

Dr. Hun's important, indeed decisive, contribution to the subject of the cortical centers of vision through his report of a case with necropsy in which a lower quadrantal field defect carefully studied and charted during life was found to correspond to a lesion sharply limited to the lower half of the cuneus.[2] In association with van Gieson, he was one of the first to define adequately the syndrome of the posterior inferior cerebellar artery [3] and to furnish a detailed topographic description of its anatomopathologic substratum. This article, moreover, contained a most exhaustive discussion of the then known physiopathology of the sensory and coordinating tracts in the medulla, and served to substantiate more especially the exact course of the pathway for pain and temperature. Dr. Hun likewise contributed many years ago illuminating articles on the pathology of myxedema and myasthenia gravis. Aside from their scientific merit, Dr. Hun's writings are noteworthy for their clearness and precision, as well as for their elegance and finish. This ability to write gracefully he probably owed at least in part to the fact that while a student at Harvard he became a pupil of Oliver Wendell Holmes, that great master of English whose lectures were such models of classic expression, and it is not surprising that the inspiration of Holmes should have found a lasting echo in Dr. Hun's subsequent pedagogic and literary efforts.

Dr. Hun's brilliant achievements fortunately did not go unrewarded. He was elevated to two of the highest positions within the gift of his colleagues, being made president of the Association of American Physicians (1910) and president of the American Neurological Association (1914), honors which come only to the privileged few of scientific preeminence. In addition, Dr. Hun was a member of the Medical Society of the County of Albany and of the State of New York, of the American Medical Association and the American Psychiatric Association.

As a citizen, Dr. Hun was vitally interested in all that pertained to the moral and educational advancement of the community in which he lived. His chief endeavors were focused on the problems which concerned the several hospitals with which he was actively connected during the greater part of his life. Being a man of broad vision and ample courage, he valiantly championed all efforts destined to improve the housing facilities and administrative policies of these various institutions, as well as to secure the most efficient and scientific service on the part of the attending medical staffs. Dr. Hun was also particularly devoted to the Albany Academy, where he himself had received his preliminary

2. A Clinical Study of Cerebral Localization, Am. J. M. Sc., January, 1887.

3. Analgesia, Thermic Anesthesia and Ataxia, New York M. J., April 17, May 1 and 8, 1897.

education. For many years, he was president of its board of trustees and worked indefatigably toward the upbuilding of the institution, a life-long effort which is known to have been crowned with success. He presided each year at the annual commencement, a function in which he took great pride and pleasure, and which furnished the occasion for some of his most scholarly addresses. He had undertaken about ten years ago the compilation of the alumni records of the school as far back as 1813 and had only recently most happily completed this monumental task.

In private life, Dr. Hun was genial and affable; he loved to play with the same spirit of candidness and enthusiasm that he displayed in the more serious pursuits of life. He was intensely solicitous for the welfare and felicity of his family, and the atmosphere of his home was one of sunshine and cordiality. A sympathetic and cheerful companion, an entertaining conversationalist and a staunch and devoted friend, Dr. Hun enjoyed the profound esteem and loyal attachment of intimates, patients and acquaintances, for he personified all that is inspiring and comforting in the make-up of a truly noble and superior person. Aside from his scientific attainments, Dr. Hun was a man of broad culture, artistic temperament and refined tastes. He was extremely fond of good drama and music, unusually well versed in literature and exhibited almost idolatry for the art of the great masters.

On April 28, 1892, Dr. Hun married Miss Lydia Marcia Hand, a sister of Judge Billings Learned Hand of the United States Federal Court in New York City. He is survived by his wife, two sons, Dr. Henry Hun, Jr., and Samuel Hand Hun, and one daughter, Miss Lydia M. Hun.

LaSalle Archambault.

Abstracts from Current Literature

ANATOMO-CLINICAL SYNDROMES OF THE STRIATE BODY IN OLD MEN. M. J. LHERMITTE, Rev. neurol. **29**:406 (April) 1922.

Some of the proceedings of the Society of Neurology of Paris are as valuable as the more formal contributions to the *"Revue Neurologique."* Those presented at a special meeting on March 30, 1922, are of such a character. Two are worthy of mention, the one noted above by Lhermitte and one on symptoms resulting from involvement of the long radicular fibers of the posterior columns of the cord by M. J. Jumentié. Lhermitte's article is of special interest. Both articles refer to the excellent work of Déjerine and were evidently the outgrowth of the Déjerine Foundation.

Lhermitte recalls how little was known about the striate body in Charcot's time, and then he speaks of the rather "feverish" work done on this subject after Mme. Vogt and Kinnier Wilson presented their views. Disorders ascribed to lesions of the striate body included anything from chorea, athetosis and the parkinsonian disease to hysteria. It is the purpose of the author to limit his discussion to studies which follow the anatomoclinical method rather than the pathologicohistologic. His patients are all old men ranging from 54 to 72 years of age. In his introduction his discussion reminds us of the method employed, or rather the approach made to the subject by Tilney in his book on "The form and functions of the central nervous system" (New York, 1921), particularly the evolutionary approach. Phylogenetically the striate body may be regarded as consisting of the paleostriatum, the mesostriatum, the neostriatum and the archistriatum. The first, in man, corresponds to the globus pallidus; the second, to the caudate nucleus and the putamen; and the third to the lenticular nucleus. Anatomic as well as phylogenetic studies confirm this division of the striate body, and are accepted, but the ontogenetic aspect is still a matter of dispute.

What the author desires to emphasize is that the embryologic relationship of the three nuclei (the pallidus, the locus niger and the body of Luys) accords perfectly with their anatomic relationship and the similarity of their pathologic reactions. It has been established that there is a very intricate and rich series of association tracts between the locus niger and the globus pallidus. It has also been established that the chemical substance of the two bodies is essentially the same. The vascular supply is also very similar in the two bodies, so much so that any lesion in the vascular tissue of the lenticular nucleus results in necrosis of other portions of the striate body. This is largely through the branches of the sylvian artery.

The author then proceeds to show how intimately interrelated are all parts of the striate body, but notes that there is an incongruity between the severity of any lesion and the secondary degeneration. He then leads up to the real thesis of his paper, the necessity of studying the lesions of the striate system not only by the aid of the myelin method, but also by the finest histologic methods which reveal the cytologic modifications of the neurons of the striate body and of the globus pallidus. Such an approach shows that interstitial and parenchymatous degeneration do not always manifest themselves in what might be termed the same ratio.

Before presenting the clinical cases, he presents the different symptoms which characterize the so-called "pallidal syndrome," and the "striate syndrome." His first chapter deals with the "pallidal syndrome." Briefly, its outstanding symptoms are the following: (1) a loss of motor activity, both spontaneous and automatic, as well as an increase in plastic tonus or flaccidity. These result in a loss of mimic movements and gesture, which in the normal person accompanies the thought processes, a lack so striking of what might be called physiologic synergy which obtains in the sum total of all movements from the simplest to the most complex. Moreover, while the elementary motor acts such as phonation, swallowing and walking, are severely disturbed, the most delicate movements, such as writing, are preserved for a long time, even when gait and deglutition are most profoundly affected. (2) In practically all the cases which the author has seen, what might be termed a tendency to overflexion is evident. This results in unusual attitudes, which, although at first they may be corrected by gentle passive movements, are resistive to all modification, due primarily to musculotendinous contractures and skeletal deformities. (3) Therapeutic agents are of little avail. Cacodylate of soda and neo-arsphenamin in large doses offer the best results, particularly with reference to the rigidity and akinesia. The effect of these drugs, however, seems to be only temporary —a few days after treatment is stopped the patient falls back into his former state. (4) A number of authors have called attention to the effect of strong emotion in these cases. The patient may under ordinary circumstances be unable to take a single step. Under peculiar stimulation he may even run or leap. Henri Claude has given to this condition the name of "tachyphemic paroxystique des parkinsoniéres." Lhermitte proposes the term "tachybrachybasic paroxystique."

From the discussion of the pallidal syndrome the author passes to that of striate symptoms following destructive lesions of the striate body. He passes over the accepted labors of others on athetosis, Huntington's chorea, etc., which ascribe the symptoms to lesions of the caudate nucleus and the putamen but not involving the globus pallidus. He refers briefly to the work of O. Foerster on the symptomatology of chorea-athetosis. He also mentions the study by himself and M. Lamaze of chronic chorea as seen in a patient whom they had observed from the second year. He particularly mentions muscular hypotonia and adiadokokinesis. In this patient the hypotonus could only be compared to that occurring in extreme cases of tabes.

It is in such cases that we get movements of greater excursion (i. e., extension) than in the normal subject. If the muscular disorder is permanent and if it does not disappear during sleep, the choreiform tendencies are increased by any psychic excitement. Andre-Thomas, Foerster and others have demonstrated that such choreiform or athetotic movements are exacerbated by contraction of the large or long muscles. Foerster has proved this by section of the motor nerve roots as well as by section of peripheral nerves, notably the external popliteal and the posterior tibial. Also, adiadokokinesis may persist after the choreiform movements are quiescent, and an adiadokokinesis separate and distinct from the cerebellar type of Babinski.

It is common knowledge that speech disturbances may be associated with chorea and athetosis. In the cases reported by Lhermitte, this becomes noticeable to the point of speech being completely unintelligible. Moreover, there is definite evidence that there is a type of dysarthria associated with the pallidal syndrome that is quite different from that associated with lesions of the striate body.

From this discussion the author passes to the syndromes of the striate body approached from the clinical and the anatomopathologic point of view based on cases studied over a period of three years. The three syndromes are (1) the syndrome of progressive pyramidopallidal degeneration, (2) the pyramidostriate syndrome and (3) the striate syndrome at the beginning of an apoplectic episode with psuedobulbar and choreo-athetotic manifestations.

The first is illustrated in the case of a man aged 58, in whom the disease began at the age of 49, characterized by hypertonicity of the left hand and of the left leg, and later involving the extremities of the other half of the body. Later there were difficulties in speech and deglutition. This condition remained stationary for five years. Anarthria and aphonia later became so complete that the patient could not utter a sound. There was also a marked dysphagia. The face was smooth and expressionless. There was no paralysis. Movements could be carried out with a certain limited force. The handwriting was correct. These facts associated with increased deep tendon reflexes, bilateral patellar and ankle clonus, as well as a double Babinski sign, made it certain that the pyramidal tract was involved. There was no tremor even after electrical stimulation.

There was no disturbance of sensibility, sphincter control or psychic function. All these symptoms taken together made it certain that the lesion gave rise to a pyramidopallidal degeneration. The process was evidently chronic, nonhemorrhagic and not involving the cord, slowly destructive, etiology unknown. The cell count and all serologic studies of the spinal fluid gave negative results.

The pyramido-striate syndrome in the case presented, as in the preceding case, apparently shows no evidence of a cord lesion. The patient was a man, 60 years of age. The first symptoms were difficulties in gait. The pyramidal signs included increased tendon reflexes, a double Babinski sign, etc. The striate manifestations included involuntary contractions of the facial muscles and of the upper left extremity, distinctly choreiform in character. There were also marked articulatory disturbances.

The third case, that of a man aged 49, presented a striate syndrome following an apoplectiform attack. After a mild and temporary left hemiplegia, psuedobulbar symptoms appeared, including dysphagia, dysarthria, short steps, panting, mild emotional instability, choreo-athetotic movements of the left extremities, muscle spasms of the left arm and leg, exacerbated by active voluntary movements on the sound side of the body. Speech and swallowing were but slightly affected.

The "fourth chapter" presents "anatomoclinical syndromes." This section or "chapter" is treated under six heads, namely: (1) the pallidal syndrome with syphilitic encephalitis of the striate body, (2) syphilitic encephalitis of the striate body in the form "rigidite des arterio-sclereux," (3) the striate syndrome of lacunar origin, (4) paralysis agitans—parkinsonian disease, (5) parkinsonian disease complicated with (epidemic) encephalitis, and (6) the pallidal syndrome with chronic arthritis deformans.

Each of these six topics are followed by illustrative cases and discussion.

Each section is illustrated by one or more cases. The first case illustrating the pallidal syndrome was that of a man aged 54. He showed all the typical pallidal symptoms, including excessive hypertonicity, fixed facies, absence of all automatic movements, spontaneous akinesia, dysarthria and dysphagia. Besides these he manifested a disturbance or loss of memory and the intellectual

faculties. The dysarthria was pronounced and nasal in character. There was excessive salivation. The patient showed a pronounced insensibility to cold. He slept with no covering except his gown in cold weather, without inconvenience or ill effect. Necropsy showed an old softening of the posterior left cerebrum. Histopathologic examination showed destruction of cells of the globus pallidus and of the putamen. There was no degeneration at the base of the peduncle nor of the internal capsule. The cerebral cortex was normal. (For some reason the author does not report the serologic findings.)

In Case 2, the neurologic findings were essentially the same, as well as changes in the psychic field.

Necropsy showed nothing grossly pathologic. Histopathologic changes were noted, however, in the putamen and in the globus pallidus. The caudate nucleus and the body of Luys also showed marked changes. Those in the locus niger were less pronounced. (Again no serologic findings are reported.)

The patient in Case 3 had intermittent vesical incontinence. The blood Wassermann test was positive. The cerebrospinal fluid had a definite lymphocytosis, 50 cells to the cubic millimeter.

The patient in Case 4 was an old chronic alcoholic, aged 66. At the age of 59 he had left hemiplegia, which completely cleared up in six weeks. He returned to work, but progressive neurologic symptoms began to appear, particularly in his gait. This was followed by weakness in the left hand, and later by bilateral adiadokokinesis,, irregularity of the pupils, acute sphincter disorders. The histopathology was much like that in the previous cases.

These four cases are then summarized.

The other five syndromes are treated in a similar manner. A brief discussion is followed or preceded by case reports. The different syndromes have many common traits and an indisputable evidence of relationship. While the pathologic processes are various, nevertheless they show that they arise from the same anatomic origin, that of the striate body, particularly the portion known as the globus pallidus.

Among the clinical physiologic symptoms common to all these syndromes, of the first importance is the spontaneous akinesia, the loss of automatic movement, the disturbance of gait and station and of the mimic and gesticulatory expression, the increase of the plastic tone with the corollaries of rigidity and fixation, cataleptic attitudes, dysarthria and dysphagia.

The condition differentiates itself from pure paralysis agitans in that the tremor is entirely absent or is transitory or intermittent. In none of the cases has "crumbling" or the pill-rolling sign been present. In contrast to this the dysarthria and dysphagia is often marked as compared with speech disturbances in paralysis agitans. In the latter there is rarely or never catalepsy, sphincter disturbances or psychic symptoms. Moreover, the progress of the disorder, so often syphilitic, is much more rapid in its course than is paralysis agitans.

JONES, Detroit.

THE NEUROLOGIC ASPECTS OF LEPROSY. G. H. MONRAD-KROHN, Videnskapsselskapets, I Mat. Naturv. Klasse. No. 16, Christiania, Jacob Dybwad, 1923. (In English.)

Monrad-Krohn bases his monograph on sixty-three personal cases. He devotes a short chapter to consideration of the pathologic anatomy of the nervous lesions. He considers that the ascending form of neuritis is the commonest although he admits that descending and metastatic forms exist. The disease

is especially apt to attack the nerve in the locus minoris resistentiae. Such places are found in the ulnar nerve behind the elbow, the peroneal nerve where it curves around the head of the fibula, and the great auricular nerve where it rides over the sternomastoid muscle. Interstitial changes are most conspicuous, but parenchymatous changes are never lacking. There seems to be no relation between the intensity of the interstitial and the parenchymatous changes, nor between them and the number of bacilli found. "The leprosy bacilli are chiefly found in the most peripheral parts of the nerves and in the inmost lamellae of the perineurium and in the endoneural septa. The parenchymatous lesion consists in degenerative changes of no specific character. The interstitial changes are very slight to start with, but may gradually lead to considerable new formation of connective tissue. . . . The formation of fibrous connective tissue will, in the course of time, press on the nerve fibers and finally destroy them. The interstitial changes may vary to a certain extent in the course of the disease. . . . Histologically, this swelling is seen to consist of a very considerable cellular infiltration of the interstitial tissue. . . . There seems to be no fundamental difference between the nerve lesions in the maculoanesthetic and the nodular forms."

The author takes up the subject of changes in other portions of the nervous system. Degenerative changes have been found in the spinal cord, chiefly in the dorsal columns. The bacilli are to be found chiefly in the ganglion cells, a few in the perivascular spaces. The spinal ganglia are also invaded and degenerative and sclerotic changes are found in the tissue. The spinal roots, the gasserian ganglion, the corpuscles of Pacini have been found affected, and Sudakewitsch regarded these bodies as the portals of entry for the bacilli. Nonspecific degenerative changes are found in the brain, and some observers have found bacilli there.

Clinically, cases of leprosy are divided into three classes, nodular, maculoanesthetic, and mixed. In many of the nodular cases however, neurologic examination will disclose anesthetic areas. "Clinical evidence seems to point to the possibility of a spontaneous cure of leprosy—or at least a spontaneous arrest in the development of the leprous lesions. When this occurs at an advanced stage, when nerve changes are firmly established, all or some of the nervous disturbances are left as permanent reminders. These cases are spoken of as 'secondary anesthetic forms' when they are the outcome of originally nodular cases."

Of the cranial nerves the fifth and seventh are most often affected, but the motor fifth seldom. All the different qualities of sensation are affected in limited fields, as a rule to the same extent, but some dissociation may occur. Occasionally some of the superficial branches (e. g. the supraorbital) may be sufficiently swollen to be plainly visible and easily palpable. Neuralgic attacks are relatively frequent, may even bring the patient to the physician for the first time.

The disturbances in the innervation of the facial muscles are characteristic. The points that distinguish this paralysis from other forms are as follows:

"(1) The upper part of the face—particularly the orbicularis oculi and the corrugator—is more often and more intensely affected than the lower part of the face. (2) This paralysis of the upper part of the face is as a rule bilateral. (3) In the inferior part of the face the supraoral muscles are more commonly affected than the infraoral. (4) This paralysis of the inferior part of the face is not so constantly bilateral as the paralysis of the upper part of the face. (5) The paralysis is accompanied by extreme hypotonia or atonia, which

causes ectropion of the eyes in a great number of cases—and in some cases where the orbicularis oris is equally affected, 'ectropion of the mouth.' This is generally accompanied by dribbling of saliva from the mouth.

"It is a striking feature of the facial paralysis in leprosy that the individual muscle is often affected in a variable degree in its different parts."

The article is illustrated with numerous sketches of patients showing these peculiar deformities. Fibrillary contractions are observed at times. "It will easily be seen that only lesions of the most peripheral (terminal) branches of the facial nerve can explain the clinical picture outlined above. I am therefore strongly opposed to Nonne's view of the central origin of the facial paralysis in leprosy." Lagophthalmos is present in from 60 to 70 per cent. of the cases, developing sometimes after a few months, sometimes only after forty years of the disease.

A complete reaction of degeneration is seldom found in the affected nerves, although the muscles will react in a variety of ways to electrical stimulation.

The great frequency of ocular lesions is due both to the imperfect closure of the lids, and to affection of the trigeminal nerve. Blindness in leprosy is usually due to affection of the cornea or iris. The extrinsic ocular muscles are seldom affected. Nerve deafness is observed, but is probably nonspecific; in the cases with advanced facial paralysis, hearing may remain good. The lower cranial nerves are seldom or never affected. The senses of taste and may be diminished but are seldom lost. Articulation is disturbed by the paralysis of the lips rather than of the other parts. Local lesions may of course determine various disturbances of speech.

In the extremities the paralysis comes on progressively with atony and atrophy. The claw hand and the simian hand develop as in progressive spinal muscular atrophy. The muscles of the arms and shoulders are seldom seriously involved. Occasionally, paralysis may develop from pressure on a healthy nerve. Flaccid, atrophic paralysis is frequently seen in the lower limbs. Coordination is affected but slightly. "It is surprising to see how deftly the patients use their paretic, atrophic and mutilated limbs at fine needlework." The gait is steady even in the advanced cases in which blindness has set in and mutilations have caused profound deformities of the lower limbs.

Paresthesias and neuralgias are frequently encountered in cases of leprosy. Hyperesthesia may precede hypesthesia. Anesthesia progresses slowly in all four limbs from the distal parts to the proximal, affecting one form of sensation more than another at times, but never presenting any complete dissociation. Sensory changes are particularly liable to develop in the distribution of the peroneal and ulnar nerves.

Sometimes the anesthesia corresponds more or less closely to the extent of the macular eruption. On the trunk the anesthetic area is always smaller than the plaque whereas on the limbs the reverse is true. Delayed sensation and improper localization are met with, but loss of the sense of deep pressure and of position is almost encountered. The sensory changes vary from time to time.

Palpation of the nerves is very important and may lead to the diagnosis, but the procedure requires practice and judgment in difficult cases.

Tendon and superficial reflexes are usually preserved.

Various vasomotor, secretory and trophic disturbances are frequent: coldness, cyanosis of the parts, anidrosis, glossy skin, pigmentations and depigmentations, even pemphigus, and loss of eyebrows and eyelashes. Perforating ulcers are frequent, panaritia and dry necrosis of bone leading to mutilations. "The most characteristic trophic disturbance is, however, the concentric atrophy

of the small bones of the fingers and toes without any lesion of the skin. This concentric atrophy consists in a gradual absorption of the bone, so that this steadily grows smaller (shorter as well as thinner), yet all the time keeping more or less its original shape. When this affects all phalanges of one finger this latter still more or less retains its shape, but becomes undersized, so much so that in fact it looks like the finger of a child grafted on the hand of an adult." Neuropathic joints may occur ,and trophic lesions of the nasal bones. The nails have a great tendency to remain, but are often thickened and deformed, cracking and breaking off.

Mental changes are only indirectly the result of the disease and depend on the knowledge of the nature of the disease and its prognosis. Occasionally, persecutory delusions are disclosed. The mental examination gives no help in the diagnosis of leprosy. All sorts of complications may occur extraneously in a disease that sometimes lasts as long as sixty years.

The differential diagnosis is based principally on the combination of cutaneous and peripheral nerve lesions, the latter being irregular in distribution, with thickening of the nerve trunks. Trophic lesions like those in leprosy are never seen in other forms of peripheral neuritis. "When one speaks of the characteristic features of an illness, I think the most characteristic findings in leprosy are the peculiar facial paralysis and the concentric atrophy of the small bones of the hands and feet. They are the nearest approach to what we today are allowed to call pathognomonic signs."

FREEMAN, Philadelphia.

TWO CASES OF EPILEPSY IN PARROTS FOLLOWING PSYCHIC TRAUMA. F. DE ALLENDE-NAVARRO (Chili), Festschr. f. Constantin von Monakow, Schweiz. Arch. f. Neurol. u. Psychiat. **13**:25-60, 1923.

The first case reported by de Allende-Navarro was that of a parrot which displayed great facility in understanding and talking. At the time of its death it was 22 or 23 years of age. Three years before the parrot had been greatly frightened by a cat that attempted to attack it while in its cage. Since this incident the parrot had behaved like a different bird and had grown to be excessively timid. Shortly thereafter it became subject to attacks in which its eyes became fixed momentarily and in which the animal trembled for several seconds. These attacks resembled petit mal. In the course of time they became more and more frequent, and shortly thereafter a speech difficulty was noted. For example, instead of saying, "Bataillon halt!" it said, "Bataillou holz!" Definite paraphasia appeared. Two and one-half years after the fright, typical epileptiform seizures appeared, which were preceded by an aura of agitation, trembling, anxious clutching of the rounds of the cage, followed by sudden falling to the floor. The attacks were nocturnal as a rule. The bird appeared to be suffering pain. It was nauseated and frequently vomited, this disturbance apparently being of a cerebral character. No paralysis or contractures were noted; however, there was marked ataxia. The bird became emotional and fearful, later apathetic and somnolent, resting immobile on its perch. It died following an epileptiform seizure.

The examination of the brain revealed marked changes in the mesostriatum. The ganglion cells were found in various stages of degeneration, distorted in shape, surrounded by satelite cells; which gave evidence of marked activity and showed neuronophagia. The vessel walls were considerably thickened; there was vascular proliferation and thrombosis. The glia cells showed marked proliferation. The ependyma, particularly of the inferior horn of the ventricle,

was markedly thickened, and there was a cellular invasion of the subependymal tissue. Here and there extravaxations of blood were found. The choroid plexus showed considerable proliferation of the glandular cells, effacement of the normal configuration of the villi and desquamation of the choroidal cells. The vessels were greatly dilated and injected.

The second bird was a parrot of the same type, 14 years of age, intelligent and well trained in speaking. There was no history of illness or other disturbance, with the exception of a psychic trauma caused by a fall into a lake. About a month thereafter, epileptiform seizures appeared. It might be said that previous to the onset of the convulsions the bird had had a nasal discharge which lasted several weeks, but which disappeared, apparently without harmful complications. A short time before death the convulsions had increased in number to twelve or fifteen a day, speech became progressively slow and ultimately disappeared entirely but without the exhibition of paraphasia. The gait became ataxic, there was dysphagia, nausea but no vomiting and finally complete anorrhexia.

On microscopic examination, changes similar to those noted in the first parrot, were found. However, these changes were slight in comparison.

The author sought to find the cause of the ataxia in the pathologic processes noted in the mesostriatum. These alterations, he thought, also explained the disturbances of speech and deglutition. The symptoms of increased intracranial pressure, presenting the picture of a pseudotumor he thought might have resulted from the hypersecretion of the choroid plexus and the ependymitis. The microscopic examination in both cases included proliferation of neuroglial elements, alterations of the choroid plexuses, of the ependyma, of nerve cells, of blood vessels and a partial degeneration of the septomesencephalic tracts.

The cause of the epileptiform seizures, de Allende-Navarro thinks was the psychic shock. He says that fright is not infrequently the cause of epilepsy in man. Of 1,440 epileptics, Moreau noted that shock was given as a cause in 314 instances. The mechanism might be explained as follows: (*a*) As a result of the shock cortical reflexes are liberated which cause a hypersecretion of epinephrin, which in turn produces a hypersympathicotonia. (*b*) The psychic trauma disturbs the ectomesodermal barrier causing a disturbance in the secretion of the choroid plexus and of the neuroglia, which in turn secrete hormones awakening the correlation of other endocrine glands, such as the thyroid and the suprarenal. In the first instance, this correlation would be purely nervous and in the second instance it would be chemical. Both factors may be present, and we may be dealing with a neurochemical process. If the shock is too violent the protective membrane, which is also known as the ectomesodermal, or hemato-encephalic barrier, which acts as a purifier, selective dialyzer and regulator, becomes abolished. The nervous elements are placed in an unfavorable milieu which disturbs their normal function and results in morbid psychic manifestations. Microscopic examination actually did reveal such an alteration. Under the influence of psychic trauma, a neurochemical mechanism calls forth a humeral correlation. Because of the disturbed hematoencephalic barrier, these substances which have been called forth penetrate and reach the nervous elements, where they result in improper function. If this barrier is not reestablished, a vicious circle results.

In discussing essential epilepsy, the author states that it has been proved beyond a doubt that a pathologic heredity is the important underlying factor. Another important aspect of the problem concerns the relation of epilepsy to the pathologic changes that have been demonstrated. Chaslin, in 1891, found

a proliferation of neuroglial cells, particularly those of the superficial layers of the cortex, which he regards as the primary lesion of epilepsy. Chaslin believes this gliomatous change is the result of faulty development. The ganglion cell changes are secondary. Alzheimer, on the other hand, believes that the degeneration of the nervous alements precedes the proliferation of the neuroglia. Bleuler, and Tramer and Weber think that the changes in the marginal glia bear a direct relationship to the degree of dementia.

The author believes these changes are of great importance in our understanding of epilepsy. The researches of the Spanish school led to a consideration of the neuroglia as an interstitial gland, analogous to the interstitial gland cells of the gonads. We are already familiar with the function of glia cells from the standpoint of nutrition, particularly during the embryologic period. In epilepsy the sclerosis of this structure interferes very much with its embryonic functions. The epileptic patient is afflicted with autointoxication from the period of birth. The author has found that the portion of the choroid plexus nearest the horn of Ammon is the most seriously involved. The lesions in the medullary substance of the horn of Ammon are secondary to those of the plexus. Briefly expressed, epilepsy is probably caused by a congenital disturbance, by the constitutional dysfunction of the endocrine apparatus; this includes involvement of the internal secretion furnished by the choroid plexus and the neuroglia cells. The disturbance of the ecto-mesodermal barrier may rest not only on a faulty embryologic development but may result from other factors such as infection, intoxication, trauma and tumors. Volhard's theory of cerebral edema in uremia is rejected by Paul de Monakow, who believes that uremia is caused by some toxic agent. The general opinion that in glial proliferation we see a constitutional anomaly is gradually gaining headway. We thus see that epilepsy and gliosis are fundamentally related.

WOLTMAN, Rochester, Minn.

THE CLIMATIC PSYCHONEUROSIS CALLED THE "NEVADA." E. ESCOMEL, Rev. psiquiat. **4**:17, 1922.

Escomel describes a psychoneurosis which he believes results from a certain climatic atmospheric condition, namely, an electrical surcharge of the atmosphere at high altitudes. This belief as to an atmospheric origin is said to be shared by several other South American observers who have studied the disorder. So common are these psychoneurotic manifestations in the higher elevations of Pèru, appearing as they do in all social strata, that local designations have been given them by the laity. Thus in Arequipa the condition is commonly known as arequipitis, in Briska as briskitis, etc. Escomel's observations were made in Arequipa, and he describes the disorder under the name of the nevada —a psychic disturbance which manifests itself coinicident with a particular state of the atmosphere, nearly always overcharged with electricity, and with the appearance of certain types of clouds in a sky which is generally clear. In Arequipa, 2,399 meters above sea level, no snow falls, although generally there is snowfall over the Nevada mountains of Chachani and Pichu-pichu as well as over the Misti volcano, points not greatly distant from Arequipa. When the snowfall is increased on these mountains there are more clouds over Arequipa, the sun is hidden and the atmosphere depressing. To this atmospheric state the aborigines have given the name nevada gruesa (heavy nevada). When there is no snowfall over the Nevadas the sun shines in Arequipa and

only a few lightly stratified clouds are seen along the horizon. This state is called the nevada rala because of the scarcity of clouds.

On certain days (during the nevada gruesa) the atmospheric condition is such that when drawing on woolen undergarments or combing the hair, or as the result of friction produced on striking the keys of a piano while playing, small electric sparks are produced. Stroking the back of a cat with the hide of a llama will produce quite large sparks. This electric state and the nevada itself will immediately disappear if it rains, also the abnormal nervous state induced by the atmospheric condition.

Apparently there is extant much of a legendary nature concerning the nevada, but Escomel does not believe that suggestion plays as great a rôle as the atmospheric condition in precipitating the disorder which he describes. He had noted early in his studies that the guinea-pigs in his laboratory during the nevada were slower in their action and lost their appetite, that his horse was more restless and that children as young as 2 years slept poorly and were peevish, quite contrary to their usual habit. This convinced him that there was something more than suggestion as an etiologic factor, since very young children and animals could hardly be subject to the suggestive effect of a legendary nevada.

No class escapes, children being affected as well as adults, but women more frequently than men, and the proportion among brain workers is greater than among common laborers. Puberty seems a trying time for both sexes; women near or during the menstrual period succumb easily, but singularly enough are relatively free during pregnancy. It is particularly marked in women at the beginning of the menopause, especially in unmarried women. If an individual or a group of persons have undergone some great emotional experience, the susceptibility is increased. As an example of group involvement, the population of Quesquena is cited. This town suffered a particularly cruel invasion from the Chileans during the war of the Pacifico, and to this day the inhabitants retain an indelible collective impression of their harrowing experiences which renders them exquisitely sensitive, not only the actual eye-witnesses, but also their descendants, to whom Escomel believes the susceptibility has been transmitted.

A typical description of the disorder is admittedly difficult to give, because of the great variety of individual reactions. One subject may be optimistic, another pessimistic; some may be dominated by various phobias, others experience just a sense of ill feeling. On the days of the nevada, some of the affected persons arise with a feeling of general heaviness and leave their beds only because some duty impels. Others experience no unusual symptoms until they have been up and about for a few hours. The subject's usual character undergoes a transformation, even his physiognomy, he may be irritable and quarrelsome. Two of the very best friends, if both be affected, may quarrel over the most trivial affair. Others are depressed; everything is gloomy; they recall to mind their dead relatives, their misfortunes, their misadventures and even think of suicide. Some are hypomanic, display more than exuberant spirits toward their friends, even toward strangers. Here, however, the reviewer is able to find exemplification of the old adage of the "ill wind," for, says the author, "if in this hypomanic state the affected person is a poet or musician he is very likely to write or compose in a most exquisite manner." Sick persons, particularly subjects of organic nervous diseases and subjects of other organic diseases, have exacerbations during the period of the nevada. There are some people in Arequipa, however, who say the nevada has little or no effect on them. This, Escomel believes, may be thus explained: either they

have not lived in the city long enough to become sensitized (two years being the minimum time required for sensitization), or they are the possessors of well stabilized nervous systems which make them immune.

If the Arequipian who suffers from the nevada should leave the city and remain away for a sufficient length of time, he would recover. On his return he would be free from the condition for a period, a certain length of time being necessary for resensitization. This is also true of foreigners whose business make residence in Arequipa necessary. The mentally gifted young Arequipian, the author believes, should not remain in Arequipa if he wishes to attain the greatest mental development, because that climate is harmful for mental workers.

Escomel says that it is doubtful whether the nevada per se is capable of producing neuropathic persons, but the repeated excitations of the nervous system may retard mental development. The children of those who suffer severely will be neuropathic. The elimination of the atmospheric condition which induces this psychoneurotic state is, of course, out of the question, so that the treatment suggested is, in short, proper mental adjustments to the difficulties of life and the selection of careers within the physical and mental possibilities of the patient. Although physical work and exercise are stressed, the physical effort must be suitable to an altitude such as is that of Arequipa.

FULLER, Boston.

HIRNTUMOR (BRAIN TUMOR). HANS CURSCHMANN, München. med. Wchnschr. **70**:1182-1184 (Sept. 14) 1923.

This article, while intended for the general practitioner, is of sufficient importance to warrant a review.

It is important to differentiate the generalized symptoms from the focal symptoms. At times focal symptoms may be absent or so slight as to be overlooked.

Headache is probably the most important generalized symptom. In a patient who has previously been well, headache suggests the possibility of a brain tumor. The various types of headache are described by the author. Associated with the headache and related to the increasing intracranial pressure, psychic disturbances, especially somnolence, also slowing of the pulse, nausea, vomiting and more rarely respiratory impairment, may develop.

Choked disk is the most important sign of pressure. A fundus examination should be made in every case of chronic headache, and more cases of early tumor would be recognized, as frequently fundus findings are the first objective sign. Occasionally choked disks do not occur, but this is not the rule, and it may be said that choked disks represent the cardinal symptom of brain tumor.

Psychic disturbances vary greatly. Apathy, which may develop into somnolence or even deep coma, is most common. Early neurasthenic symptoms of various types, hysterical reactions, or even psychotic manifestations of mild cyclothymic schizophrenia, general paralysis or presbyophrenia, may present themselves. According to Curschmann, psychic manifestations, especially in brain workers, are not infrequently the first general symptoms.

Dizziness may be either a generalized symptom or a focal symptom. As the former, it may be constant or periodic. Convulsive attacks at times occur as generalized symptoms and have no localizing value. On the other hand, jacksonian attacks naturally are of focal significance.

Generalized symptoms, as a rule, are not of long duration. They tend to come and go and not infrequently are replaced by added signs. Often both

generalized and focal symptoms are exaggerated by apoplectic attacks. These are the result of hemorrhage into the tumor. It is important that focal signs should occur rather early and be of considerable duration. Transient palsies are always to be looked on with misgivings as to their focal significance.

As important focal signs the author considers:

1. Localized pain and tenderness over the skull.

2. For the side of the tumor the author refers to the beginning unilateral choked disk. This he believes is especially true in an uncertain posterior fossa. tumor.

3. Jacksonian convulsions.

4. Roentgen-ray and pneumoencephalography. Dandy's procedure is not looked on with favor, but the lumbar route is considered less dangerous and better for diagnostic results. Under the heading of localization the author takes up:

1. Motor area. Nothing of special importance is brought out under this heading.

2. Frontal region. Right-sided tumors may run a symptomless course beyond a few generalized signs. In left-sided lesions, apraxia and ataxia may occur. Psychic manifestations of marked variability present themselves. The much referred to "Witzelsucht" is not frequent. Disturbances of intelligence, lack of attention, somnolence, etc., may be present.

3. Third and fourth ventricle tumors. Various motor disturbances, diplegias and tetroplegias may occur. Ocular phenomena in tumors of the corpora quadrigemina are the rule. Visual and auditory disturbances and trunkal ataxia may occur from neoplasms in this region. In fourth ventricle tumors the author has occasionally seen generalized epileptic attacks.

4. Cerebellum. Generalized symptoms are the rule and occur quite early. Unilateral ataxia or asynergia with nystagmus of especially the affected side, past pointing, unilateral hypotonia and hyporeflexia are rather the rule. Cranial nerve involvement is naturally important, and an absent corneal reflex should not be overlook. In case of vermis lesions, unilateral symptoms may be absent. Stiffness of the neck and cervical pain are important in all posterior fossa tumors.

5. Cerebellopontile angle tumors. Acoustic tumors present a characteristic syndrome frequently with the absence of choked disk. There is hypacusis or anacusis, vestibular syndromes, anesthesia or pain in the distribution of the fifth nerve (rarely sixth and seventh nerve involvement) and crossed pyramidal signs.

6. Basal tumors. Unilateral cranial nerve palsies are the rule. Pituitary tumors belong in this group with well-known hemianoptic findings. The author mentions the Tween brain syndromes, which are probably the result of injury to the subthalamic region rather than distinct pituitary disturbances. Psychic manifestations may also occur in this group.

7. Pons and Medulla. In this region tumors are rare. Tuberculomas are most common. Generalized symptoms may be few, choked disk usually absent; hemiplegia cruciata inferior is the usual early pontile syndrome. Tumors of the peduncle lead to hemiplegia cruciata superior. Multiple sclerosis, syphilis and small vascular lesions are not to be overlooked as possible causes

of affections in these areas. Medullary tumors are difficult to differentiate from progressive bulbar paralysis. It is well to bear this association in mind.

Gliomas are probably the most common form of brain tumor. Less common are sarcomas. Tuberculomas are not uncommon, especially in the cerebellum and pons. Carcinomas are rarely primary; endothelioma and psammoma are among the rarer neoplasms.

The therapy, while usually surgical, should not be urged without due thought, as in the author's experience the mortality is about 60 per cent. even in the best of hands. The use of roentgen-ray therapy should not be overlooked, especially in osteosarcoma and endothelioma.

In passing, the author warns against the indiscriminate use of lumbar puncture in brain tumors, especially in posterior fossa lesions.

MOERSCH, Rochester, Minn.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Jan. 17, 1924

JULIUS GRINKER, M.D., *President, in the Chair*

REPORT OF A FAMILY EXHIBITING THREE CASES OF CONGENITAL OPHTHALMOPLEGIA. DR. HARRY R. HOFFMAN.

After briefly reviewing the literature on this subject, Dr. Hoffman presented the cases of a mother and two children. The family history of the mother revealed nothing of importance. Both children were illegitimate and by different fathers. In all three, the ophthalmoplegic condition had been present without change since birth. The mother had had generalized convulsive seizures since the birth of the second child four years before. The mother, aged 33, presented bilateral ptosis; the pupils were equal and regular and reacted to light and in accommodation; there was hypotrophia of 10 degrees; the lateral movements of the eyes were free; the superior and inferior recti on both sides were completely powerless; the fundi were normal; there were slight nystagmoid oscillations on lateral movement; the results of blood and spinal fluid examinations had been negative, and the mental age by intelligence tests was 9 years and 10 months. The elder boy, aged 14, was unable to move the eyes in any direction, had bilateral ptosis, equal pupils that reacted normally and normal fundi. The younger child, a girl aged 4, presented an ophthalmoplegic condition exactly resembling that of the mother.

DISCUSSION

DR. GEORGE W. HALL: I think that some of these cases are related to primary muscle disease rather than to nuclear involvement. My reason for making this statement is that I have seen on three or four occasions a boy about 12 years of age with progressive muscular dystrophy, who presents eye changes similar to those presented here, which, according to his mother's statements date back to early life.

DR. PETER BASSOE: I do not quite understand why Dr. Hall thinks that the affection in these children is related to muscular dystrophy. There has been no progression as there would be in dystrophy. It might be pure muscular defect, but I understand from Dr. Hoffman that an ophthalmologist has found that the muscles are all present. The most reasonable assumption would be that there is a congenital absence of part of the nuclei. This condition of congenital nuclear ophthalmoplegia seems to exist in a great many races. A few months ago I ran across the report of a similar family in China. The author could get no history of other cases in the ancestry, but he added that this was not peculiar, for while the Chinese love to record the glories of their ancestors, they never mention their defects.

DR. HARRY R. HOFFMAN: There have been no other pregnancies, and the pupils all react normally.

A Case of Family Periodic Paralysis. Drs. John Favill and Charles F. Rennick.

This report appears on page 674 of this issue.

DISCUSSION

Dr. H. Douglas Singer: In the case that I observed many years ago, the attacks were usually complete, although there were slighter attacks. Dr. Favill mentions increased epinephrin secretion as a possible cause for the attacks. This is difficult to accept; the unstriated muscles, as a rule, are not involved, and severe sweating is common. In the patient I observed, the heart dilated markedly and the condition sometimes became alarming. This was particularly true in one attack in which there was paralysis of the levatores palpebrae. The attacks seemed to me to be due to some toxic action on the muscles. On that view, I experimented with diuretics and with restriction of water. The results were striking. While taking diuretics, no attacks occurred during a considerable period. When restricted to a limited amount of water, one attack occurred after another. On resuming the diuretics, the attacks again disappeared.

In that case and in two others seen since, muscular work unquestionably brought on attacks. In the two later cases, the attacks were all mild and of short duration and could be brought on at any time by sending the boys out for a walk. In these two brothers, diuretics apparently had no effect, but there was a definite relation to muscular effort. This has been observed in many cases in the literature.

Dr. Favill: I should have mentioned that these cases occasionally end fatally. Holtzapple noted six deaths, one of which he saw occur during an attack, in the family he recorded. Fortunately for our patient, his family has a type of the disorder which apparently becomes less severe as time goes on. Every case has become less marked, including his own.

Brain Changes in Typhus Fever. Dr. G. B. Hassin.

This paper was published in full in the Archives, February, 1924, page 121.

A Method of Determining the Mental Age During a Physical Examination. Dr. David M. Levy.

This paper appears on page 669 of this issue.

DISCUSSION

Dr. H. Douglas Singer: It seems to me that this method of testing will be of great value. Dr. Levy has been conservative in his claims. I have had an opportunity to look over his figures and was much struck with the results obtained. It is a method which can be used for making a rapid estimate when no other means are available, and it has the advantage of avoiding the calling of the patient's attention to the fact that a mental test is in progress.

Dr. Herman M. Adler: I wish to say a word on the bearing of this test on the problem of intelligence. Dr. Levy has pointed out that this test correlates well with the Stanford-Binet scale, but that it probably does not test intelligence. There is room for further study along these lines, which may throw light on the significance of the intelligence tests. Psychologists are at present earnestly discussing the whole subject of intelligence. They started out by calling the Stanford-Binet and similar tests, tests of intelligence, but of late a good deal of

doubt has come up as to whether they really test intelligence. One of the most recent statements is that we do not really know what these tests do test; it was worded rather quaintly "that these tests measure whatever it is that they do test."

This work of Dr. Levy on behavior tests supplements that of Dr. Franz of Washington, who has produced some remarkable results in the reeducation of paralytic persons in whom nerve cells in the cortex were definitely destroyed, but who were trained to carry out quite complicated actions, such as playing a game of baseball. This meant that an entirely new set of neurons was trained to take up the work of the destroyed cells and throws new light on the older ideas of restricted localization. More recently experiments have been made by Dr. Lashley of Minneapolis with white rats with the cortex entirely removed. In spite of this mutilation they could be trained to carry out complicated behavior reactions, such as solving maze puzzles.

President Scott of Northwestern University has said that the so-called intelligence tests do not measure intelligence but are tests of alertness. This work of Dr. Levy raises the question whether his tests and some of the intelligence tests are not really tests of maturity. Ordinarily the state of maturity is correlated with the development of other functions, mental and physical, so that in most instances the results of the test may be assumed to indicate intellectual maturity and ability and therefore possibly intelligence, although they may not directly test for this.

In the physical field, roentgen-ray studies of the bones of the hand have been made by Dr. Rotch of Harvard on the basis of which the actual physical age can be determined regardless of the chronologic age. Anything that will help to determine the age of the person in terms of development rather than in years of life is extremely valuable. It is possible that Dr. Levy's tests may indicate something of this sort and certain behavior reactions are characteristic of a state of development rather than of the particular experience. Such information is always of value in disentangling the rôle of the environment in development. It seems unlikely that the responses to Dr. Levy's tests could be determined by the environment. They seem to represent a stage of development. It is interesting and encouraging to know that we can analyze behavior by such simple tests as these when formerly we could do so only by complicated methods.

In Memoriam

The following resolutions were presented and adopted unanimously by rising vote:

Whereas, It has pleased God in His infinite wisdom to remove from us our fellow member, Harold N. Moyer; and

Whereas, The Society in him has lost one of its founders and guiding spirits, a faithful attendant and contributor to its proceedings, who served twice as its president, who gave liberally to his fellow members both of his professional knowledge and his personal charm; and

Whereas, The insane of the state in him have lost a friend who began his service to them in his youth as physician in a state institution and carried on his activities in their behalf as an educator, reformer, counsellor in legislation, consultant and student; until the last in active attendance as consulting physician to the Cook County Psychopathic Hospital; and

Whereas, Midwestern neuropsychiatry has lost from its midst a man not only learned and skilful in his specialty but by virtue of his broad interests,

culture and literary ability, an unequaled interpreter of neuropsychiatric and medicolegal problems for the public at large whereby he furthered the best interests of mental hygiene; and

WHEREAS, The Society feels that in his death it has lost a friend, distinguished in his chosen field of medicine, beloved for his genial personality, and admired for his personal integrity; be it,

Resolved, That the members of the Chicago Neurological Society express their sorrow and extend their most sincere sympathy to the family and friends of Dr. Moyer; and, be it further

Resolved, That copies of these resolutions be sent to his family, to the ARCHIVES OF NEUROLOGY AND PSYCHIATRY, to the *Journal of the American Medical Association,* to the *Journal of Nervous and Mental Diseases,* and to the *American Journal of Psychiatry,* and that a copy be preserved in the archives of this Society.

Regular Meeting, Feb. 21, 1924

JULIUS GRINKER, M.D., *President, in the Chair*

PSYCHIATRIC PROBLEMS IN A PENITENTIARY. DAVID P. PHILLIPS, JR.

At the Illinois State Penitentiary, Joliet, the usual examinations covering physical, mental and social characteristics are made on all prisoners entering the institution. The type of training instituted is based on the physical and mental health, as well as individual qualifications. More importance is now attached to character building than to the mere serving of time. As far as possible, there is segregation of the feebleminded and borderline cases, with special supervision and training for these groups. Definite psychotic cases are usually transferred to other suitable institutions. Recommendations are made in all cases of persons appearing before the Divisions of Pardons and Paroles. Special attention is given to prisoners showing inability to adjust themselves properly under disciplinary treatment.

The patients constituting the main psychiatric problem are those classified as having a psychopathic personality. These patients show a definite trend toward some behavior difficulty. In the classification used, three principal groups are recognized: the inadequate, the egocentric and the emotionally unstable. The diagnoses are based: first, on evidence of a definite trend; second, on evidence of repeated difficulties with environment and third, on evidence of the salient characteristic that is common to all difficulties in the same case.

Approximately 10 per cent. of the entire prison population shows some degree of maladjustment under disciplinary treatment. These men are the offenders against the prison rules; they are punished for their violations and are considered the most important prison problems. The types of violation committed are varied, with, however, only a small percentage of those of major type. These offenders during the past three years have shown definite characteristics that differentiate them from the other inmates. There has been a steady decrease in the number of violations of prison rules during the past three years, although the total population has increased, and the methods of punishment used have become less severe. We now feel that the person who constantly violates the prison rules is in need of medical care rather than of severe punishment. Statistical comparisons are of interest: Prisoners with higher grades of intelligence

have the most difficulty in adjusting during their imprisonment; the feebleminded and borderline persons react best under supervision; recidivists include a high percentage of violators of prison discipline; first term prisoners, as a rule, get along well, a fact that accords with the idea that "old timers" make little or no effort, or are not as capable of getting along well either in penal or civil life. Offenders against discipline are usually between the ages of 20 and 25 years. Prisoners with a positive history of syphilis, head injury, or chronic alcoholism, usually do not get along well in prison life. Few men with a history of syphilis have received treatment prior to admission. A high percentage of the offenders have at least one of these physical conditions. Cases of psychopathic personality form about 80 per cent. of the entire group of behavior difficulties. Subdivision of these personality cases indicates that the egocentric person is the most consistent violator of prison rules.

Mental disease is diagnosed in about 5 per cent. of the prison population. These cases constitute a rather definite problem, although the behavior of the men in prison has been fairly good. The state hospital for the criminal insane at Menard has a limited capacity, is always overcrowded and is not modern in any respect. Consequently, certain types of cases cannot be sent there, and it has been necessary to care for most cases of mental disease at Joliet where about seventy-five have been cared for. In the prison hospital, five cells are set aside for observation and treatment. This necessitates placing some patients in the cell houses or elsewhere during observation periods. A large percentage of the persons with mental disease have had the condition prior to admittance, and should have been committed to a state hospital rather than to prison.

A complete report is made on every prisoner appearing before the parole board. This contains all available information regarding physical and mental health, behavior reactions, etc. In addition, a recommendation is made regarding the final disposition of each case. Some may be recommended for release, others for further supervision, and others for transfer to other institutions. These recommendations are not always followed, but there has been close cooperation in feebleminded, borderline, psychotic and sex delinquency cases.

During the past three years, there has been a decided increase in the percentage of cases making a successful parole. During the year 1923, approximately 87 per cent. of the prisoners paroled made good; that is, they completed their parole without further difficulties and were discharged. Practically all of the 13 per cent. of failures were persons with a psychopathic personality. Copies of the case reports made by the mental health officers are given to the parole agents having charge of the paroled men. This enables them to recognize the type of shortcoming that the prisoner formerly exhibited, and also helps them to continue the supervision and training already started in the institution.

Drug addiction, which is usually such a great problem in most prisons, causes little concern. Only 0.8 per cent. of the population at the Joliet penitentiary can be classed as former addicts. It is interesting to note that the majority of these patients are admitted from Peoria and Decatur; only a small percentage come from Chicago.

When the mental health program was first established at the Illinois State Penitentiary, the reaction of the prison officials was one of tolerance with some distrust. Gradually, as the benefits of this work were recognized, more cooperation was obtained. At the present time, most of the problems in the institution are acted on first by the mental health officers. The psychiatrist acts in an advisory capacity to the prison staff, as well as to the deputy warden, in the dajly prison court.

DISCUSSION

DR. HUGH T. PATRICK: How does Dr. Phillips account for the extremely low percentage of drug addicts from Cook County in the whole population at the penitentiary? That was to me a surprising statement.

DR. GEORGE W. HALL: How does Dr. Phillips account for the improvement in these cases during the last three years, that is, the number of persons that have gone out and made good in comparison with the previous statistics?

DR. DAVID P. PHILLIPS, JR.: The cases of pandering mentioned were not sent to the penitentiary. Cases of this type are sent to the Bridewell, and are not under our jurisdiction.

In most cases admitted to the penitentiary for a sex crime, a rather extended period of incarceration follows. There have been a few prisoners released by the parole board that we felt should have been required to serve longer sentences. The usual minimum time served by men sentenced for sex crimes is from four to five years. The maximum time served depends largely on the type of crime committed and the sentence that crime carries under the statutes. When there is a record of previous difficulties of sexual nature, and examination reveals a low intelligence rating, the parole board takes only one action—it pronounces the maximum sentence. Near the expiration of that sentence, the case is referred to the division of the criminologist for further action, and a commitment to some other institution usually follows.

I am at a loss to explain the low percentage of drug addicts. In the examination of the prisoners, the history is obtained from the inmates, from the court records and from the social service department of the division of the criminologist. The percentage quoted was based on this information. I suppose that many of the Cook County drug addicts are sent to the Bridewell, and others may be convicted of federal charges, such as violation of the narcotic laws, and are sent to federal prisons.

Regarding the increase of successful paroles, there has been an increase in the number of parole agents during the past three or four years, with a corresponding perfecting of the entire parole system. At this time the state is divided into twenty districts. Each district has at least one parole agent, and there is more careful supervision of the men after they are released. Then too, the cases that the mental health officers recommend should not be released are those of men who would be unable to make a successful parole, and this tends to increase the proportion of successful paroles.

MENTAL RATINGS BY GROUP TESTS. SIMON H. TULCHIN (by invitation).

Little need be said about the necessity for studying the individual school child in order to place him in the grade for which he is best fitted. There is general agreement on this point. The disagreement lies in the selection of methods to be employed. The problem is not only to select the feebleminded, but also to select the superior child. When one examines the wide range of chronologic ages and of mental ages in any classroom it becomes apparent that uniform methods of instruction must necessarily fail to produce the best results.

The great majority of superior children are to be found in the schools, but the selection of the feebleminded is suggested in a number of ways: (1) Feebleminded children can be referred by the homes. Through this method, however, only the idiots and the lowest grade defectives—the children that do not get to school—will be selected. There may be a small percentage of high

grade defectives also kept at home, but these are generally children of well-to-do parents who can afford to pay for private tutoring. The cases referred by the homes would constitute a very small percentage of the feebleminded. (2) Another source of reference is the physician. Here again the majority of cases would be low grade defectives and the total percentage of cases thus referred small. (3) A considerably greater percentage of cases would be referred by various social agencies. But the objection mentioned above holds true even here, for it is only the low grade defective that is brought to the attention of the social agencies. The high grade defective would still remain a problem. These three methods should be used as supplementary in order to reach the children who are not in the schools. (4) Another method of selection—advocated by many—is the selection of feebleminded children by the school teacher. This method has its advantages: first, because the teacher through her daily association with the children is able to make observations of the child's school progress and general behavior; and second, because the teacher comes in contact with practically all children of school age. Actual experience, however, shows that this method is not satisfactory. It lacks uniformity. The criteria of feeblemindedness are likely to vary from teacher to teacher. Even if such criteria were supplied from the outside there would still remain the personal bias in their interpretation. The teacher is apt to be prejudiced and use other than objective methods for her selection, and she is likely to lack the special training required to recognize the high grade defective and refer only the low grade defectives. This last point is not necessarily a reflection on the teacher. As a matter of fact, the more intelligent and the more careful the observer is, the more likely he is to hesitate to classify any doubtful case as feebleminded. Experience has shown that the teacher is likely to consider the child primarily, and sometimes only, in reference to classroom performance. Thus it happens that a child who is as much as two or three years retarded according to his chronologic age, but is able to carry on the work of the grade he is in, is not considered retarded by the teacher. The same is true for the superior child, the child who by chronologic age is far above his grade; being above his grade he does not especially stand out when his school performance alone is considered. Thus it frequently happens that a high grade defective is actually rated as superior by the teacher because he is able to carry on the work of the room, the teacher failing to consider that chronologically the child should be two or three years higher, and the superior child is rated as average, the teacher again not considering the chronologic age. The teacher is also likely to overlook the "nice" and the "passive" defective—the child who never causes any difficulty and always seems to be working hard. (5) Another possible selection and certainly the most desirable one is the selection by means of individual study. To make the study complete, each child should be examined at the time of school entrance. This would make possible not only the selection of the feebleminded but also the proper placement of the superior child. This method would require much more time than can at present be given. It would also require a great deal of money, although not nearly as much as is being spent on keeping children more than one year in the grade; that is, children who are low grade in intelligence and have to repeat a grade, or children who are superior and could progress at a much faster rate than one year per grade. The real difficulty, however, is the fact that such examination would require experts, and at the present time the experts are few. (6) The method which will probably best answer the need is the method of selection by means of group tests. Group

tests, if well standardized, will select the feebleminded as well as the superior child. They take little time to give and score, they are objective, and they are relatively inexpensive. They should be used, however, only as a method for selection and not as a method for final diagnosis, because the group tests are unfair to the shy child, the nervous child, the indisposed child, and fail to disclose the child who is copying or malingering.

Such a method for selection—the group test method—was employed in a recent survey of a school system in three cities in Illinois conducted by the Institute for Juvenile Research. The facts presented are based on results obtained from a study of fourteen public schools and one high school, a total of over 3,500 children. The findings were illustrated by charts and tables:

1. A comparison was made between teachers' estimates of intelligence and the intelligence ratings found by tests. The teachers were also asked to classify the children in three groups: sympathetic; unsympathetic, and annoying. The chart showed that while in the sympathetic group, the teachers' estimates of intelligence arrange themselves in a fairly regular distribution with about 50 per cent. falling into the average group and the remainder equally divided between the superior and inferior groups; in the unsympathetic group, 66 per cent. are classified as inferior, and in the annoying group, 80 per cent. are classified as inferior. Out of 100 cases in the unsympathetic and annoying groups, only one case is classified as superior. These facts point out some of the difficulties involved in making the selection of cases through the teachers. They show that the teacher's selection is founded to a great extent on an emotional basis. The same chart also shows that on the whole in the sympathetic group the teachers tend to overestimate the superior and to underestimate the inferior groups; whereas, in both the unsympathetic and annoying groups, the teacher overestimates the percentage in the inferior groups.

2. The range of chronologic ages in each grade is wide, with the median ages of 6½ for the first grade, and 8 for the second, 9 for the third, etc.

3. The medians of the mental ages in each grade are somewhat lower in the first three grades, but are practically the same as the chronologic medians in all other grades.

4. The curves of distribution for males and females run closely together. The distribution is very regular with a high point for the group adequate in intelligence and about equal percentages for inferiors and superiors.

5. There seems to be a steady increase in the superior groups and decrease in the inferior groups from grade to grade, except in grade 6 in which the inferiors increase and the superiors decrease. This is probably due to the fact that a number of the schools have only six grades, and hence there is an accumulation of inferiors to give them a chance to graduate and to obtain work certificates.

6. In the high school a comparison between the freshmen and seniors reveals that among the freshmen there is a much greater percentage of inferiors and a much smaller percentage of superiors than among the seniors. The distribution of the entire high school shows that only 2.7 per cent. are classified in the backward group, all others being either adequate or superior.

It is found that those who speak English at home rate higher than those who use a foreign language. The only fair comparison of nationality is the one that compares only groups using the English language in the home.

THE USE OF THE POLYGRAPH IN THE STUDY OF FALSIFICATION. JOHN A. LARSON (By invitation).

By analysis of respiratory and cardiac curves, obtained with the Erlanger sphygmomanometer, it has been possible to demonstrate significant changes that result from deception in actual police court and Institute for Juvenile Research cases. In all cases, the experimental results were obtained from cases of known deception in which there was real emotion involved, and usually something was at stake, such as the life or liberty of the subject, in contradistinction to cases of deception in the university laboratory in which the emotions involved are probably not comparable either in degree or intensity. That the fear of the innocent, or his anger when unjustly accused, or the skill of the recidivist, do not interfere with this test as much as commonly thought, has been shown by the experimental results. Subjects of all types and ages have been used, varying from the innocent man who has been positively identified and apparently proved by the evidence to be guilty, to the juvenile delinquent aged 6 who was lying about sex or some delinquency. In all cases, however, the subject was sufficiently aware of his deception to show emotional disturbances which were recorded by the graphic methods.

Aside from the detection of lying in the case of the juvenile offender who denies any sex experience or some offence mentioned in the history, the knowledge of which is essential to the psychiatrist, it is also important to be able to detect malingerers. In addition, by the same technic and a suitable questionnaire it may be possible to detect and unravel complexes; this has actually been done in the cases of young children. The following two cases will illustrate: A boy, aged 14, explained episodes of running away as the result of being more or less influenced by a voice which he would hear clearly as though someone were in back of him or on the side of him; this voice always said — "Let's go" — whereon he went. The problem was to determine whether this boy was malingering or whether he had actually experienced these auditory hallucinations. His record when tested seemed to indicate deception, and he later admitted that he had never heard any voices and was merely trying to keep the psychiatrist from discovering the real facts of the case. A boy, aged 11, insisted that he had seen God on several occasions, and described these occurrences with great detail. An analysis of the case revealed that instead of being hallucinatory, these experiences had no actual existence but were in the nature of a wish fulfilment; he said he had been told that, if he were good, under certain conditions he would see God and on every occasion mentioned by him God had only seemed to appear after he had been wishing to see him; in every instance he was in bed, and in all but one case his eyes were closed. The record of this boy showed marked disturbances when he was questioned as to whether these occurrences had actually happened, and the many contradictions and confused statements of the boy later revealed the fact that he did not believe in them himself. It finally developed that these occurrences had been suggested to him by relatives and that his manner of describing them varied according to the questions of the examiner.

In summing up the results in deception during the past three years the following conclusions seem warranted:

1. The analysis of cardiorespiratory graphic records obtained during deception in which there is a real emotional element seems to be of more value in the detection of deception than a study of reaction times, qualitative nature of the reply, or increase in the systolic blood pressure. It has been possible to differentiate the records of guilty suspects from those of innocent suspects, although

the life and liberty of the individuals were involved. It has also been possible to differentiate the record of a person when lying from that of the same person when telling the truth.

2. The nature of the reactions under emotional stress have varied with the individual; thus, in one person there may be an excitation, as shown by increased frequency, greater amplitude, and so forth, while in another there may be a depressing or inhibitory effect.

In an attempt to determine the degree of reliability to be placed on such a test, there should be a careful standardization of thousands of records obtained from all types of persons, normal and abnormal. The results obtained up to date by various investigators are sufficiently hopeful to encourage and stimulate intensive research in this direction. Instead of offering such objections as, "Why study the graphic changes, or quantitative fluctuations in the blood pressure when the respiratory quotient should be studied and exact measurements made in the oxygen metabolism during deception?" efforts should be made to determine the validity of the present methods which seem suggestive. Having determined the relative accuracy of present methods of attack, other technic may be resorted to.

On considering the relative values of the different methods employed in the study of the deception complex, the present method, that is, the use of the polygraph, which should include blood pressure curve, seems superior to such methods as those used in the association reaction time, for it affords a permanent and objective record. The questions can be recorded automatically on a revolving kymograph, and all that is necessary for the examiner is to adjust the blood pressure at a given level and start the cylinder revolving. Regardless of the interpretation made by the examiner, the record secured will be a permanent and faithful reproduction of the changes that occurred in the subject in response to the experimental stimuli. Through the use of this or a similar technic, it may be possible to overcome to some extent the resistance of the subject and thus secure his cooperation.

DISCUSSION

DR. LEWIS J. POLLOCK: Perhaps the remarks which I may make are not applicable to the exact title of Mr. Larson's paper, yet I feel they are pertinent to the method of examination. Some years ago, Dr. A. H. Dollear and I made a study of emotional reactions in catatonic dementia praecox, employing pneumomographic and sphygmomanometric tracings. In such cases, in which gross physical as well as psychic stimuli produced no apparent outward manifestation of emotion, many interesting records were obtained of involuntary expression of such emotion. We employed, as did Mr. Larson, an Erlanger sphygmomanometer which gives continuous tracings and demonstrates relative changes in blood pressure. Whatever may have been the character of the emotion elicited, the reactions to this emotion were made evident by this method. It was interesting to note that physical stimuli, such as noise, flashes of light, odors, pain, etc., produced a lesser reaction than did psychic stimuli. Various psychic stimuli were employed, such as the calling of the patient's name, ridiculous statements, accusations, repetition of family history, the elision of expected numerals in a sequence, etc.

In contradistinction to the cases of dementia praecox, the tracings in a case of hysterical obtusion in a murderer showed absolutely no change in the respiratory curve or blood pressure as the result of either physical or psychic stimuli. The psychic stimuli in this instance included the accusation of com-

mitting the crime and a description of the crime. It would appear, therefore, that the defect in emotional expression in the latter case is in the afferent and in the former in the efferent arc.

It may be of some interest to know that Dr. Dollear was called as an expert witness in a case of an aged man who had murdered his son, shooting him because of a minor infraction of home discipline. No reaction of respiration or circulation was demonstrable when the shotgun with which he shot his son was shown him or newspaper clippings were given to him to read, or when he was reproved for his crime. The tracings obtained by Dr. Dollear were introduced as evidence at the trial, and the man was acquitted of murder and adjudged insane.

DR. MEYER SOLOMON: Is it not true that with a normal person under stress and strain, or emotional upset, you can have variations of the type here demonstrated?

DR. LARSON: The objections will be discussed in the order in which they were presented:

1. The statement that the cardiac curve shown is merely a pulse curve and does not represent a continuous blood pressure curve is apparently due to a lack of familiarity with the literature.

2. The objection that not sufficient controls were obtained in no way concerns the actual experimental procedure. For demonstration it was unpractical to treat the material in any other form, as representative sections of each phase were shown for the purpose of comparison. Obviously all the material could not be shown in any case. Of course, the normal of the lying suspect can only be obtained after the confession.

3. The statement that this work is too empirical in its nature and that, owing to the intricate mechanism involved in an emotional reaction, such as deception, it is impossible to label a given disturbance a lie, is of theoretical interest only. In every case shown it was possible to differentiate the portions of the record in which deception occurred, as checked, from the rest of the record, or the record of the lying subject from that of the truthful one. How great a percentage of accuracy can be obtained can only be determined by intensive investigation. The factors and explanation of the changes underlying these disturbances which occurred during deception may be obtained by subsequent investigation, if possible.

4. Such objections as the fear or anger of the innocent suspect as vitiating factors in a deception test can only be properly evaluated by actual experimentation. In the cases cited and others, it has been possible to control these factors so that a correct interpretation has been obtained, although in some cases the life of the suspect has been at stake.

Regular Meeting, March 20, 1924

JULIUS GRINKER, M.D., *President, in the Chair*

A CASE OF HYSTERICAL HEMIPLEGIA WITH A NEW METHOD OF TREATMENT. DR. MEYER SOLOMON.

This man, aged 56, was a city fireman. At the time of the accident which led to the present illness, he was planning to leave for a pleasure jaunt to

which he was looking forward with great expectation. He denied any cause for anxiety or dissatisfaction.

On the evening of Aug. 8, 1923, he was assisting in pumping out a basement that had been flooded. In lowering the suction hose into the basement he received what he believed was an electric shock in his right hand, and quickly dropped the hose. His fellow worker refused to believe that he had received a shock, and the patient, thinking he was perhaps mistaken, again took hold of the pipe, and again felt a strong shock in his right hand. He staggered to one side, and, as others came to him, fell in a heap and, in a dazed, dreamy condition was taken to hospital. Next morning his right arm and leg were paralyzed, felt numb, and sensation was lost, especially in the leg. He was in bed for about six weeks and his condition improved somewhat, especially in the right hand.

He came under my care early in October, 1923. The chief feature in the treatment has been what I call psychomotor exercises, such as shadow-boxing, fencing, punching the bag, skipping the rope and playing pool. Considerable improvement has followed, but he stopped the exercises of his own accord, and his condition has remained stationary since.

His present condition shows no evidence of organic disease. The right leg is dragged forward from behind and not through an arc. The right toe is used excessively in walking. The right knee jerk is definitely exaggerated. The right arm and leg are at times flaccid, and later spastic. There are astereognosis, ataxia and loss of joint and muscle sense on the right side with paresthesia and pain.

I am convinced, from what the patient has said, that he is looking forward to and is definitely planning retirement, after being disabled for one year, with a pension.

The pains are located at the points of origin and insertion of muscles and tendons.

Ordinary routine exercises have their place in these cases, but the patient should be given exercises in which he is occupied with the task itself rather than with the movements involved.

HAROLD NICHOLAS MOYER. DR. HUGH T. PATRICK. Published in the ARCHIVES, April, 1924, page 462.

TREATMENT OF GENERAL PARALYSIS: A PRELIMINARY REPORT ON THIRTY-SIX CASES. DRS. CHARLES F. READ and HARRY A. PASKIND.

A group of twenty patients with general paralysis have been treated with tryparsamide at the Elgin State Hospital since July, 1923. The majority of these patients have had two courses of eight doses each (3 gm.), together with weekly injections of mercuric salicylate (0.06 gm.). Sixteen patients have received two courses of eight doses of sulpharsphenamin (0.4 to 0.8 gm. weekly) together with mercuric salicylate 0.06 gm.

Remissions thus far secured in either group do not surpass the percentage that may be expected in cases in which the patients are treated in the usual manner with arsphenamin. The improvement in physical health in the tryparsamid group has been notable; many negative blood Wassermann reactions have also been obtained, but no negative Wassermann reaction in the spinal fluid. Several cases of apparent early optic atrophy (one or two of them evident) have been found in both groups, although the patients in the tryparsamide group were the only ones examined at the beginning of treat-

ment. Some of the patients treated with sulpharsphenamin have also made marked improvements (one remission), but 25 per cent. are worse than at the beginning of treatment, whereas none in the tryparsamide group have apparently deteriorated.

Though somewhat disappointed in the present results, the reporters realize that they have had to do with types unfavorable for treatment, and that it is too early to draw conclusions as to the results of this effort. In justice to the remedies employed, another six months must elapse before publishing results in detail.

DISCUSSION

Dr. David M. Levy: Mental tests have been made on these patients, and their value as an indication of the improvement is worth consideration. The difficulties in the control of attention and in cooperation were such that an accurate mental age was difficult to determine. The variations in testing the same subject over twenty-four hours might be considerable. In one case there was a difference greater than the probable error of the test within six hours. However, when cooperation could not be secured, at least, to cover all the tests attempted, i. e., when a score could not be determined for that particular time, it was struck out entirely. Since the usual error of a test is considered to be at least six points in terms of intelligence quotient, we should certainly not consider a change of less than ten points above or below the original score as having any significance. On that basis six cases in the group, seventeen in all, showed significant changes for the better in their scores; one, more than 20 points increase in the intelligence quotient and five, from 10 to 20 points increase. The remaining patients showed in general an improved score, with not one case of a drop; i. e., as far as the tests can determine anything. There was not a high correlation of these improved scores with clinical improvement. More striking than the increased score was the improvement in cordiality and general attitude during the reexaminations.

The striking response of the patient with general paralysis to the Stanford-Binet test is the marked scatter. This averaged, as in Dr. Well's series at the Boston Psychopathic Hospital, over seven years. A patient passing all tests on the sixth year level would commonly make successes up to the sixteenth year. This is a greater range than in any other group, even in dementia praecox. However, its significance must be checked against a control group of normal adults of the same age, the median of which is about 47.

The lowest scores for the group were with the digit tests, especially repeating three digits backward: A few could not repeat forward after me 9-2-8, a digit span repeated by children aged 3, and yet these same patients were able to do vocabulary tests on the eighteenth year level. Most specific to this group was the inability to copy simple designs from memory, a test on the tenth year level. Not one of the seventeen was able to do this perfectly in the first examination, and there was least improvement on retests.

Dr. Clarence Neymann: Since July, 1923, Dr. Singleton and I have treated about twenty-five patients with this disease in the Edward Hines, Jr., hospital. Most of these patients have now had two courses of treatment and are beginning the third. Some, therefore, have had sixteen and some about twenty injections of tryparsamide. There was a six weeks' interval of rest without treatment between the courses. Generally speaking, eight patients are strikingly improved. The clinical material differs radically from that of Dr. Read. The cases fall generally into the group of syphilis of the central nervous system.

Only about one-third are cases of outspoken general paralysis. The group of cerebrospinal syphilis includes some patients with general paralytic colloidal gold curves and four plus Wassermann reactions with the spinal fluid, with the onset of clinical symptoms from one to three years after infection. Such cases have shown marked improvement. One patient with optic atrophy just barely had light perception when we began treatment. He still has light perception. Thus far we have noted no bad effects on the optic nerve. Several of these patients with cerebrospinal syphilis had been treated with large amounts of arsphenamin before we began treatment with tryparsamide and had not greatly improved under this treatment. Mercuric salicylate was given once a week three days before injections of tryparsamide.

Dr. Peter Bassoe: During the past five or six months I have administered about 150 doses of tryparsamide. It is too soon to speak of permanent results, but I have seen striking improvement in several cases. I have been particularly impressed by the case of a man with general paralysis who came under treatment in January, 1922. He was then unable to work and presented the usual clinical and laboratory signs. He improved decidedly on the Swift-Ellis treatment, but early in 1923 he relapsed, and six subsequent Swift-Ellis treatments produced no improvement either clinically or serologically. He then received eight injections of tryparsamide, and toward the end of the course he was well enough to return to his former occupation. Last January, the Wassermann reaction for the first time was negative with both blood and spinal fluid. There was no increase in cells or globulin, and the colloidal gold curve was only of a weak tabetic type. Since then the patient has had another course of tryparsamide and remains well.

Another case showing striking improvement is that of a man, aged 60, who has an old tabes and last summer developed a psychosis which I at first considered an involutional melancholia; last autumn he had two epileptiform convulsions which, in spite of his age, made the case look like one of taboparesis. After a course of eight injections of tryparsamide, there was marked physical and mental improvement, and the spinal fluid became normal. However, I have also had cases in which little or no improvement has been noted. I had seen no ill effects on the eyes until two days ago, when two patients under treatment, one a tabetic, aged 70, the other a general paralytic in the fifties, complained of sudden visual impairment. In one case, central vision was greatly impaired in one eye, while the other patient had extreme concentric narrowing of the fields with good central vision. No patient should receive this treatment unless not only ophthalmoscopic but also perimetric examination has been made beforehand.

Dr. Lawrence J. Hughes (by invitation): I think some of these patients were not examined before the treatment was started. In the other group we examined them, but the fields have not been taken. These patients will not cooperate readily. The only thing I can speak about is the ophthalmoscopic appearance of the disk and the vessels as they appeared from time to time. I finished examining the last group last week and was struck with the number of patients in whom there was a marked alteration in the fundus changes as compared with those present before, not only with the tryparsamide but also with the sulpharsphenamin treatment. These vessels, particularly the arteries, were small and thread-like, and there was a disproportion between the artery and the vein. In a large percentage of the cases, I think there has been definite ophthalmoscopic change in the fundus before the clinical signs of optic atrophy have appeared. In this treatment, fundus examinations

must be made from time to time, and when we find a fundus with marked vessel change we should stop treatment for a while at least.

Dr. Read: I want to refer again to a patient (tryparsamide group) who presented practically a disappearance of the colloidal gold precipitation, together with greatly modified spinal fluid findings. This man attained by the Stanford-Binet tests a 15 year level, but remained in an apathetic dementia praecox-like state. It has been quite striking that all patients in the tryparsamide group express a subjective sense of improvement. Part of this may be due to general paralytic optimism, but the patients are unanimous about it.

It is rather striking that while those on tryparsamide have either remained stationary or have improved, of those receiving sulpharsphenamin 25 per cent. show further deterioration. We regret that we did not have a control group for the psychometric tests. This should have been done. We emphasize the fact that the visual acuity must be determined from time to time and that the chart test alone cannot be depended on. Dr. Lorenz has called attention to the fact that in a number of his cases vision has become stabilized at a lower level—has diminished somewhat and then remained stationary.

Seasonal Curves in Mental Disorders. Dr. Frank P. Norbury.

1. Climate is a seasonal factor in the etiology of mental disorders.

2. Mental disorders are affections of the brain with predominating but not exclusive psychic symptoms.

3. Exhaustion of human energy is a formidable factor in all forms of mental disorders.

4. Exhaustion involves more than innate brain instability.

5. Climate as an environmental factor has potentials which affect the standards of sanity.

6. Standards of sanity depend on environment, which varies not only with the standards of civilization but with the climatic factors on which such civilization depends.

7. The standard of sanity depends also on the standard of the individual. The standard of the individual involves heredity, circumstance and environment.

8. Human energy is not dependent on climate alone, but climate is a potential factor in the standard of the individual.

9. Mental disorders in their mental mechanisms showing exhaustion parallel the seasonal curves of efficiency as delineated by Huntington.

10. These seasonal variations in mental disorders show a gradual increase in incipient or recurrent cases from January (the low of the curve) to June (the high of the curve), with a second curve, showing low in August and September, with the high in October, November and possibly December.

11. The data thus far studied warrant the deduction that climate and seasonal diseases contribute to the etiology of exhaustion, which is the primary factor in producing mental instability—the borderland of mental disorder. One patient may be inherently in the borderland all his life. Another may only be so when physical or mental stress precipitates him into this zone. Another may, by more violent mental cataclysms or more stressful bodily exhaustion, as from disease or accident, be impelled into the borderland and beyond to the realms of defined mental disorder, known as insanity, there to remain in the acute stage until it has run its course. And whether recovery takes place, or death, or chronicity follows, depends on factors, essentially clinical that belong to the field of neuropsychiatry.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Feb. 21, 1924

C. MACFIE CAMPBELL, M.D., *President, in the Chair*

AN UNUSUAL CASE OF PISTOL-BULLET WOUND. DR. J. W. COURTNEY.

A man, in the late forties, one evening in December, 1923, was shot at close range with murderous intent. There were powder stains on the victim's face. The bullet carried away the two upper median incisors, ploughed a furrow along the upper surface of the tongue and clipped off the uvula. A roentgenogram taken at the hospital shortly afterward showed the bullet, which was of heavy caliber, in contact with the anterior surface of the body of the second cervical vertebra. There were no cord symptoms of any kind or degree, and surgical intervention was not indicated. Some days later an abscess began to point along the outer border of the upper third of the right trapezius. This was later evacuated by Dr. H. H. Germain, who at the same time tried unsuccessfully to get the bullet. A roentgenogram taken after this intervention disclosed the fact that the bullet had disappeared. It showed also some evidence of structural damage to the body of the axis. The proximity of the original site of the bullet to the esophagus suggested that the missile had dropped into the stomach. As a matter of fact, the roentgen ray located it in the cecum. The stools were watched, but the bullet was not recovered. Nevertheless, a further roentgen-ray examination showed that it had been eliminated. The patient was discharged directly his operative wound healed. He has recently returned to the hospital, with increasing stiffness of the neck and severe pain which radiates along the course of the occipitalis major on either side. Neurologic examination was negative except that the palatal reflex was abolished, speech was nasal and deglutition painful. There was little or no febrile reaction.

My feeling was that we were dealing with a traumatic osteomyelitis of the axis, but a recent roentgenogram provided no conclusive evidence on this score.

Ultimate Outcome: No notable changes occurred for a fortnight or longer. Against advice the patient then went home, where subsequently he died. Necropsy disclosed a purulent necrosis of the entire axis and a partial destruction of the third cervical vertebra. There was in addition a generalized purulent meningoencephalitis.

SYMPOSIUM ON PITUITARY DISEASE. PRESENTED BY MEMBERS OF THE PETER BENT BRIGHAM HOSPITAL STAFF. GROUP A. ACROMEGALY. DR. TRACY PUTNAM.

The history and clinical course of an acromegalic patient operated on three days previously by Dr. Cushing revealed the bony and sellar changes typical of the condition. He complained chiefly of extreme weakness and lassitude. On two occasions he had had a transient temporal hemianopia of the left eye. He was given two therapeutic roentgen-ray treatments, with marked improvement in his symptoms. He was then sent home, and received at another clinic a third roentgen-ray treatment. After this treatmnet there was almost immediately a great decline in vision, and he returned here for observation. When no improvement occurred after two weeks he was operated on by Dr. Harvey

Cushing by the transphenoidal route, and a portion of the soft hypophyseal struma was removed. Microscopic examination of this material showed almost complete necrosis. There was rapid return of vision following this procedure.

GROUP B. DYSPITUITARISM WITH PITUITARY ADENOMA AND LARGE SELLA. DR. GILBERT HORRAX.

CASE 1.—M. S., a woman, aged 45, entered the hospital complaining of failing vision. Her family and past history were irrelevant. Three years before she began to notice a gradual loss of vision in the left eye, which progressed until one year ago, when it was noted that vision on the temporal side of the left eye was entirely gone. At this time vision in the right eye began to fail, and continued to a total loss of the temporal field on this side also. She had not menstruated for three years. Physical examination showed the presence of bilateral primary optic atrophy and a typical complete bitemporal hemianopsia. The roentgen-ray showed a deep, irregular sella, with marked erosion of the posterior clinoids. The basal metabolic rate was 19 per cent below normal. A transphenoidal operation with evacuation of a considerable amount of soft pituitary adenoma was performed by Dr. Cushing on February 18. The patient showed an immediate improvement in vision, with demonstrable widening out of the right temporal field.

This case is typical in all respects of the group of patients presenting indications for a transphenoidal operation rather than an operation from above, the choice being made on the basis of a generally enlarged sella, without evidence of calcification either within or above it. In this connection, attention was called to another case in the hospital showing the same clinical picture as the preceding patient. In the patient referred to, a previous intranasal operation had been performed on the basis that her symptoms were caused by some local condition. This previous operation, with removal of the septum, made it impossible to carry through the transphenoidal operation, an attempt at which had to be abandoned.

CASE 2.—E. N. G., a man, aged 25, came to the hospital, complaining chiefly of loss of vision in the right eye. Except for a tendency to epistaxis during the past six years, his history was negative. His present illness began two years before with frontal headaches and gradual failure of vision in the right eye. He noted from the outset that he could not see objects on the outer (temporal side of the right eye). This failure of the right eye had progressed steadily up to the present time. In July, 1923, a right turbinectomy was performed for relief of vision, without effect. During the past three years he had gained 30 pounds (13 kg.).

Physical examination revealed a moderately obese person with soft smooth skin, the hair and fat distribution over the body being distinctly of the feminine type. His beard was scanty. There was a well marked primary atrophy of the right optic disk and a slight pallor of the left disk. The visual fields showed the retention of only the upper nasal quadrant on the right, with a normal field for the left eye. A roentgenogram of the skull showed a generally enlarged and deep sella turcica, with extremely thin posterior clinoids.

This patient illustrates an outstanding hypopituitarism of the syndrome adiposogenitalis with a large sella undoubtedly containing a soft adenoma or so-called chromophobe struma. He was awaiting operation by the transphenoidal route and was believed to be an ideal case for this procedure.

GROUP C. DYSPITUITARISM WITH SUPRASELLAR (CRANIO-PHARYNGEAL POUCH) CYST.

CASE 1.—T. H. C., a child, aged 5, was referred to this clinic because of headache, vomiting and blindness. The child's early development was apparently normal. Diminution of vision was first definitely noted when he was 2 years old, i. e., three years before, and at the same time it was seen that his eyes were becoming "crossed." Diminution of sight progressed to complete blindness by October, 1921, although he was still in good health and active. Fourteen months before the child had vomiting spells and was drowsy during one week, and then was again active and bright until seven months ago. From this time until the present he has had continued headaches and vomiting and marked loss of appetite, and has been emaciated, drowsy and generally weak.

Physical examination revealed an emaciated and extremely lethargic child who could not be aroused by any ordinary stimuli. There was conjugate deviation of both eyes to the right with continuous nystagmus in this direction. Both fundi showed the presence of complete primary atrophy, on which certain pressure changes had been superimposed. Stiffness of the neck was marked, and Kernig's sign was positive. A roentgenogram of the skull showed marked convolutional atrophy and a large, ballooned out sella with thinned posterior clinoids. Within the sella there were multiple, small dense shadows of calcification, which were believed to be in a suprasellar cyst.

On February 19, the cyst was tapped by Dr. Cushing through a single burr opening in the skull. Following this procedure the child responded and took nourishment. Further taps of the cyst are contemplated with a view to improve the patient's general condition sufficiently so that a frontal operation can be performed and the cyst radically removed.

Obviously in cysts above the sella, the only approach which offers any possibility of removal is an intracranial operation. The frontal lobe can be retracted and the tumor exposed to some degree. In certain instances a complete enucleation of the cyst with its contained calcifications can be accomplished.

The following case illustrates the same type of condition in an adult. This patient was in the early stages of pressure, having headaches and choked disks. No specific glandular manifestations were present.

CASE 2.—S. J. C., an Italian laborer, aged 30, whose family and past history were negative, had an illness that began one year before with frontal headaches —supraorbital—which had continued. There had also been tinnitus in both ears, and during the past six months an increasing unsteadiness in gait. He had complained at times of a burning sensation on the left side of his face.

Physical examination revealed slight bilateral exophthalmos, early choked disks, more marked on the right, and a relative hypesthesia of the left cheek. A roentgenogram of the skull showed in addition to marked convolutional atrophy, a deepened, irregular and eroded sella, with some probable areas of calcification just above it. The basal metabolic rate was 14 per cent. below normal.

This patient is awaiting operation. This case again illustrates the type of condition best dealt with by a frontal intracranial procedure.

HISTOLOGIC ANALYSIS OF FORTY-TWO CASES OF ACROMEGALY. DR. PERCIVAL BAILEY.

In this report are presented the results of a histologic analysis of a series of forty-two cases of acromegaly from which material had been removed at operation. This material, consisting of fragments of the hypophysis, had been fixed

immediately, and so was suitable for a microscopic study. The material had been fixed in three different fixatives—Bensley's, Zenker's, and 10 per cent. formaldehyd, with the exception of the more recent ones, which have been fixed in Regaud's fluid.

It is important to investigate alterations of the structure of an organ by the same methods used for the demonstration of its normal structure, as well as by the use of methods for displaying pathologic substances. The essentials of staining methods as applied to the pituitary gland are the necessity of avoiding acids and sublimate mixtures as fixatives, and of employing specific dyes for the demonstration of the granules. An optimum procedure consists in fixing the material in Regaud's fluid and staining by means of ethyl violet-orange for the alpha-granules and with acid-violet for the beta granules. Double staining of the two granules in the same preparation may be done by the use either of Bailey's acid fuchsin-acid violet combination, or safranin acid-violet combination of Maurer.

From a study in this manner of all the material available, and a comparison of the results with the Zenker and Bensley fixed material, it is concluded that the hypophysis of acromegalic persons shows definite histologic characteristics by means of which it may be identified.

Book Review

LECTURES ON ENDOCRINOLOGY. BY WALTER TIMME, M.D., Attending Neurologist, Neurological Institute, New York; Professor of Endocrinology, Broad Street Hospital; Professor of Nervous and Mental Diseases, Polyclinic Medical School and Hospital. Price, $1.50. Pp. 123, with 27 illustrations. New York City: Paul B. Hoeber, Inc.

In the flood of recent literature on the endocrine glands, some of it vague and theoretical, some just superficial and unpractical and some of it mendacious advertising, this little book with the rather pretentious title is a great comfort. As the author states, it is not quite up to date, being "an unchanged reprint of an article which appeared in 1921." But it is a lucid and fair statement of what we know or nearly know of the functions and disorders of the endocrines, and we know of no work presenting so much information in such small compass.

An outline of the function of each gland of internal secretion is sketched, and in succession are described the clinical syndromes of subinvoluted thymus, precocious involution of the thymus, abnormal pineal involution, hypothyroidism and hyperthyroidism, suprarenal dysfunction, pituitary disease and gonad disorder. Of course, polyglandular disease or disorder comes in for frequent consideration.

The author accomplishes the feat, often difficult for one intensively working in a new field, of being honest with himself. He is alive to the contradictions and the enormous lacunae in our knowledge of the glands of internal secretion and fully aware that the interpretation of clinical pictures frequently is difficult or impossible. Nor does he claim miraculous or even astonishing therapeutic results.

He promises a more complete work in the future. It is greatly to be desired, and doubtless will avoid the few unimportant inaccuracies of this booklet and be provided with better illustrations.

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